THE
BRITISH JOURNAL OF SURGERY

VOL. XLIV MARCH, 1957 No. 187

CANCER OF THE TONGUE

A STUDY BASED ON 653 PATIENTS

BY SIR STANFORD CADE AND E. STANLEY LEE
WESTMINSTER HOSPITAL, LONDON

INTRODUCTION

IN 1927 a paper by Arthur Evans and Stanford Cade was published in this JOURNAL entitled "Cancer of the Tongue: Preliminary Report on Radium Treatment". Thirty years have since passed, and the possibilities of the methods there described have been continuously and systematically studied by one of the authors of the original report and his colleagues. The total experience up to the end of 1955 amounts to 653 cases (*Table I*). The majority

Table I.—MATERIAL

Number of Cases of Carcinoma of the Tongue 1925–55 inclusive

Male	508 (78 per cent)
Female	145 (22 per cent)
TOTAL	653

of these have been treated in Westminster Hospital, London, but all others treated in various institutions and privately have been included.

The common factor is that all patients in this series have been under the clinical control and observation of the authors and their colleagues. The entire consecutive experience is presented, no case, however advanced, having been rejected as unsuitable for some kind of treatment. Carcinoma of the back of the tongue and vallecula are included, and some overlap with mouth floor cases and faucial cases is inevitable. This contrasts strongly with some of the published surgical series, in which the advanced cases have obviously been filtered off before reaching the Surgical Department and others have been excluded as inoperable.

The experiences of the past thirty years have enabled us to formulate answers to some of the questions relating to the indications and contra-indications of radium therapy, its advantages and disadvantages as compared with surgery, and the relative values of the various techniques of radiotherapy. The years have seen great advances, both in surgery and in radiotherapy, and it is the purpose of this present paper to review and analyse our experiences in the light of these changes and to set forth our opinions on the present position of the therapy of carcinoma of the tongue.

I. MATERIAL

Aetiology.—The age incidence and average age of our cases (*Fig.* 547) agree closely with those recorded in other series, and do not seem to have varied during the thirty years of our experience. In the sex ratio, however, there has been a striking

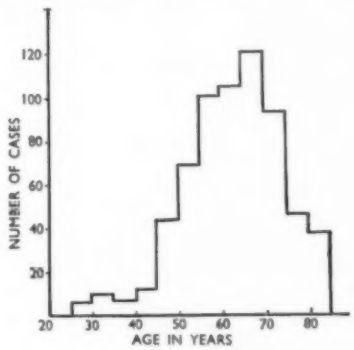


FIG. 547.—The age distribution and average ages of 653 cases of carcinoma of the tongue.

change, shown in *Table II*: whereas in 1925 10 male cases were seen for each female case, this figure has gradually fallen to 2 to 1 in the period 1951–55.

Table II.—MATERIAL

Changing Ratio of Male to Female Cases

1925–29	10 : 1
1930–34	5 : 1
1935–39 (war years excluded)	4·5 : 1
1946–50	2+ : 1
1951–55	2+ : 1

Fig. 548, based upon the Registrar-General's Annual Statistical Review, shows the total deaths, male and female, from carcinoma of the tongue, year by year in graph form. It is at once apparent that the steady fall in the total deaths notified has been entirely on the male side, while the numbers of female cases have remained almost constant for

thirty years. This change may be related to the comparative rarity to-day of that type of gross leucoplakia in men associated with a positive Wassermann reaction and severe oral sepsis. A positive Wassermann reaction is now unusual, and the mouth may be clean and even edentulous.

In other published series the proportion of male cases to female varies. It is highest in Scandinavia, and this is said to be due to the high incidence in

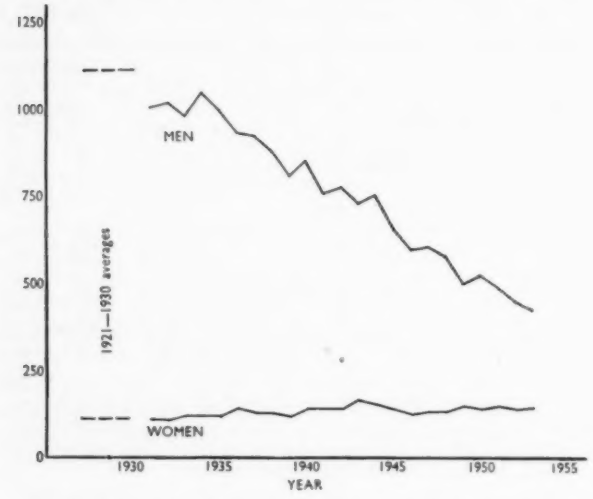


FIG. 548.—Graph showing that the reduced incidence of carcinoma of the tongue is due entirely to diminishing numbers of male cases. The annual totals for females have remained almost constant.

those countries of the Plummer-Vinson syndrome of sideropenic anæmia. This syndrome is characterized by a low level of protein-bound iron in the serum. Anæmia is usually, but not constantly, present. Jacobsson (1948), of the Stockholm Radiumhemmet, considered that of 126 women with lingual cancer 24 per cent had definite, and a further 12 per cent probable, sideropenia. In our own series the finer tests for this condition, such as the estimation of the serum-iron content and barium radiograph of the pharynx (Waldenström and Kjellberg, 1939), have not been carried out, and it is therefore probable that minor cases of this syndrome have been overlooked. Other aetiological factors such as alcohol, tobacco, septic teeth, and trauma are occasionally conspicuous; but it is notable that in many cases in recent years these factors are absent. Minor degrees of leucoplakia, often of bizarre and patchy distribution, are still common and occur in both sexes; but there is usually no obvious cause. Often the mucosa of the rest of the mouth appears quite healthy. It is clear that other aetiological factors, so far undetermined, are at work.

The incidence of multiple primary growths in the tongue itself or in the tongue and other parts of the mouth is now well known (*Table III*). Such lesions may appear simultaneously or at intervals varying from a few months to many years. The multiple lesions are found not only in cases where leucoplakia and erythroplasia are present and acknowledged as a possible precancerous state, but also in healthy, often edentulous, mouths where the mucous membrane shows no detectable abnormality. Cancer of the posterior or pharyngeal portion of the tongue, like epithelioma in the pharynx, occurs in tissues which appear to be normal as well as in the atrophied mucous membrane of the Plummer-Vinson syndrome. Family histories are not uncommon and in this series of patients there have been several cases in brothers (two of mouth cancer in twins), in sisters, and in siblings (Cade, 1953).

Table III.—CASES WITH MULTIPLE BUCCAL TUMOURS (27 *Cases*—4·1 *per cent*)

CASE NO.	SEX	AGE	SITES OF TUMOURS	AETIOLOGY?
28/11	M.	56	Lip/tongue	Leucoplakia
28/21	M.	60	Tongue/fauces	Syphilis
29/22	M.	51	Tongue/soft palate	
29/25	M.	60	Tongue r./mouth floor l.	Leucoplakia
29/27	M.	62	Tongue/lip	,,
29/45	M.	60	Tongue/tongue	,,
30/ 5	M.	54	Tongue/tongue	,,
30/27	M.	73	Tongue/lip	
31/ 2	M.	73	Tongue l./fauces r.	
31/16	M.	65	Tongue postr./tip	
33/17	M.	60	Tongue/tongue	Syphilis
33/19	M.	?	Alveolus/r. tongue/l. tongue	Leucoplakia
34/ 1	F.	69	Tongue l./soft palate r.	
34/ 2	M.	?	Tongue midline/tongue edge	Syphilis
35/ 4	F.	71	Tongue/tongue, 2 in. apart	Leucoplakia
37/12	M.	58	Tongue l./alveolus r.	Syphilis
37/16	M.	45	Tongue/palate and uvula	Alcohol
37/19	M.	56	Vallecula/uvula	
38/ 1	F.	67	Tongue/alveolus and cheek	Leucoplakia
38/13	M.	51	Tongue/soft palate	Syphilis
43/ 3	M.	58	Tongue postr./floor* (OES.)	
49/26	F.	58	Tongue/antrum	
50/11	M.	69	Tongue/lip	Syphilis, Tobacco Alcohol
50/30	M.	56	Tongue/tongue/cheek	Leucoplakia
51/ 3	F.	68	Tongue/tongue	,,
52/10	M.	80	Tongue/lip	
53/ 8	M.	73	Tongue/tongue	Syphilis

Leucoplakia = Leucoplakia without syphilis.
Syphilis = Positive blood, or clear history of syphilis.
* This patient died of carcinoma of the œsophagus.

The natural history of the disease has also changed somewhat with the passing of years. Thus visceral and skeletal metastases, rare in the pre-radiotherapy period, are now well known. Metastases in the lungs, liver, and other viscera are recorded; skeletal metastases in the femur, humerus, vertebræ, skull, and the phalanges have been seen (*Fig.* 549). Possibly the control of the primary lingual lesion and hence the elimination in many cases of sepsis, pulmonary infection, and hæmorrhage as a cause of death directly related to the uncontrolled primary lesion, may account for this.

Staging.—In an attempt to display the quality of our material we have subdivided the cases according to the size of the primary growth and the state of the lymph-nodes. The time-honoured terms 'early' and 'late' applied to a growth are of very doubtful value and we have avoided them, substituting the terms 'small' and 'large'. Reliable statements as to length of history have proved so rare that we have come to ignore this feature. The size of the primary tumour bears, of course, no constant relation to the state of the lymph-nodes, and both factors seem about equally important in prognosis. A diameter of 2 cm. for the primary tumour has been taken quite arbitrarily as the boundary between small and large growths, though

Jacobsson (1948) used 3 cm. as his dividing line and Baud (1950), at the Curie Foundation, Paris, classified her 1000 cases into groups according to the diameter in centimetres. Lymph-node involvement has been based on a clinical appraisal which, though subject to considerable error (Tailheffer, 1952), is the only practical method of initial staging.

The subdivision of our material according to these criteria is set out in *Tables IV a, b*. It will be seen that in only about half the cases was the primary lesion still confined to the tongue; in at least one-third it had spread to adjacent structures, usually fauces or mouth floor.

Table IV.—Staging of Cases

a. The Primary Lesion: All Cases

Lesions confined to the tongue :—		
Small (less than 2 cm. diam.)	121 (18 per cent)	
Large (more than 2 cm.)	214 (33 per cent)	
Total		335 (51 per cent)
Lesions not confined to the tongue		214 (33 per cent)
Unclassified :—		
Recurrent	84 (13 per cent)	
Multiple	17 (3 per cent)	
Not stated	3	
Total		104
		653

b. Lymph-nodes: Cases treated before 1951

No clinically malignant nodes when first seen :—		
Never developed nodes	89 (17 per cent)	
Nodes appeared later	97 (19 per cent)	
Total		186 (36 per cent)
Nodes when first seen		298 (57·5 per cent)
Not classified		34 (6·5 per cent)
		518

From *Table IV b* it is seen that well over half of the cases (57 per cent) had clinically malignant lymph-nodes when first seen. Of the remaining 43 per cent about half developed lymph-nodes later. This agrees well with the equally unselected series of Jacobsson, in which the incidence of lymph-node involvement at the start of treatment was about 50 per cent.

The clinical material in some other series seems to have been rather more favourable than ours. For example, Hayes Martin (1951) at the Memorial Center, New York, reported 60 per cent of cases with no initial lymph-node involvement. Others have been less fortunate. Gibbel (Gibbel, Cross, and Ariel, 1949) for instance, whose cases were drawn from a Veterans' Administration Hospital, found only 31 per cent free from nodes initially. His series was remarkable in other ways: the incidence of syphilis was very high (22 per cent of the patients) and the response to treatment was poor.

Pathology.—

1. *Clinical Type of Growth.*—Growths, are described in our records as proliferative, ulcerative, and nodular or infiltrative. That the distinction is not always clear-cut is shown by the illustrative cases in *Fig.* 550, A–G; and on review these descriptive categories prove to be of limited prognostic value. Only in broad terms can it be said that proliferative tumours are more radio-sensitive while the nodular and infiltrative types are more resistant. This is probably due to the relative vascularity and to the proportion of fibrous tissue present. Radiosensitivity must not of course be confused with radio-curability.

2. *Histology.*—All but 8 of the tumours were squamous carcinoma. The exceptions were 1 lympho-epithelioma, 2 transitional-cell carcinomas,

Fig. 549.—Radiograph showing metastasis in the iliac bone from carcinoma of the tongue.

1 angiosarcoma, 3 adenocarcinomas, and 1 probable plasmacytoma. The degree of differentiation of the squamous carcinomas we have not found of great prognostic value. It varies from place to place in the same tumour and may be differently assessed by individual pathologists. Tumours described as anaplastic tend on the whole to be more malignant, faster growing, and more radio-sensitive, but the differences are not constant enough to form a basis for treatment or prognosis. Nor does the speed with which metastases occur depend very obviously on the histological grading of the primary tumour.

These observations on the correlation between histological grading, immediate response to radiation, and prognosis only became obvious when a large series of cases was available for study and on a critical analysis of the results of treatment throughout the whole period of the disease, from onset to either complete regression or the eventual death from disease.

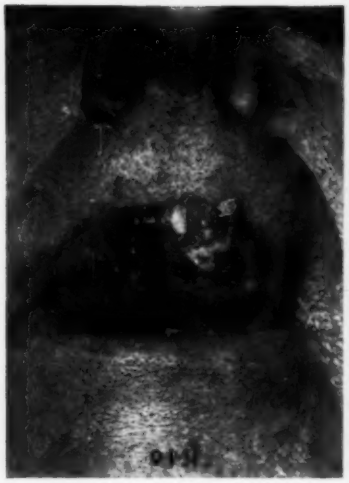
Diagnosis.—*It is a fair statement that in Great Britain to-day the commonest ulcer of the tongue is cancer.* Dental and traumatic ulcers, gumma, tuberculosis, infection around a foreign body, and actinomycosis may all cause occasional confusion,

A

D

B

C



E

but there is seldom any real difficulty in prompt diagnosis if the above statement is borne in mind. For very small incipient lesions an excision biopsy with the diathermy of the whole lesion is the proper procedure, but this is best carried out in the therapy centre. Periods of observation whilst the patient is

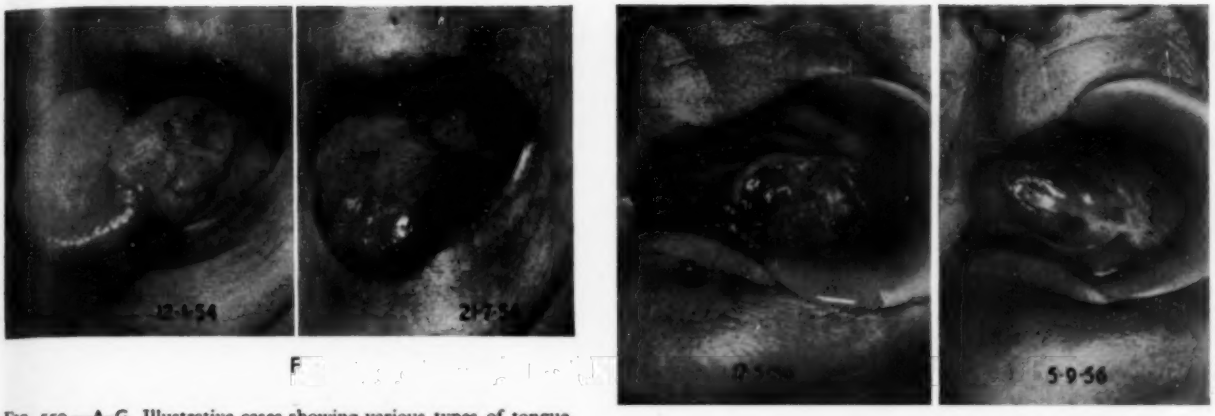


FIG. 550.—A–G, Illustrative cases showing various types of tongue carcinoma before and after treatment.

given antibiotics should not delay biopsy by more than a few days. Neither should a positive Wassermann reaction delay biopsy whilst antisyphilitic remedies are given. Yet even now there is often a delay of three to six months before a patient reaches a hospital where definitive treatment can be undertaken and adequate facilities for all methods of treatment are available.

Biopsy.—The value and safety of this procedure are no longer controversial for the tongue and in principle it should always be done. We have seen no harm in thirty years' experience provided that adequate treatment followed promptly. We strongly

FIG. 551.—Syphilitic glossitis with warty areas and fissures. In such tongues, now rarely seen, carcinoma readily arises.

deprecate, however, the performance of preliminary biopsy by clinicians not themselves intending to carry out the treatment. Such a biopsy is all too often followed by prolonged delay before the patient finally attends for therapy and may seriously affect the prognosis. The main danger of a biopsy, however, is the equivocal, or negative, report. Unless it provides some satisfactory alternative diagnosis for the lesion such a report should be disregarded, or the biopsy repeated. There are two conditions in which malignancy is often reported as doubtful: the papilloma, and the warty or fissured lesion of chronic superficial glossitis (*Fig.* 551). Here, again, the limitations of biopsy should be recognized and if there is any real doubt the lesion should be treated as malignant. We have seen a number of cases in which a report that malignancy was doubtful was tragically followed in due course by the death of the patient with local and metastatic cancer.

II. TREATMENT

THE PRIMARY LESION

The period under review has seen many important changes in this field. Radical surgery has become much safer, and consequently far more ambitious. The usefulness of teletherapy has been much enhanced by more powerful sources and more penetrating rays. Interstitial therapy, too, has seen important advances and refinements of technique. Its accuracy and precision have been improved by better anæsthesia, and the uniform distribution of the irradiation has been facilitated by the contributions of Paterson and Parker (1938, 1948) and others to the physics of the method. Useful alternatives to radium needles and radon seeds as sources have been evolved, such as radio-cobalt needles, which can be made curved, and radio-gold 'grains', which have the advantage of very small size. Tantalum wire has been used in a few cases, but is difficult to implant accurately (*Fig.* 552, A–D).

Our policy throughout the period under review has been to use implantation as the main method of treatment in lesions of the anterior two-thirds of the tongue. It is quick and safe and a high dose can be given with minimal tissue damage. The restoration of function is very much better than with radical surgery, and the statistical results are at least as good as those of surgery when we consider that the cases are entirely unselected. The photographs (*Fig.* 550, A–G) show some typical cases before and after

implantation to illustrate the good functional and anatomical results. Teletherapy became the method of choice in lesions of the posterior or pharyngeal portion of the tongue. Excisional surgery, either radical or palliative, was reserved for primary resistant and recurrent cases.

condition. The implantation itself is always carried out under general anæsthesia with an endotracheal tube and a throat pack. The needles are inserted according to a plan prepared in advance in conjunction with the physicist, and each needle is carefully sutured into place. Premature falling out of needles

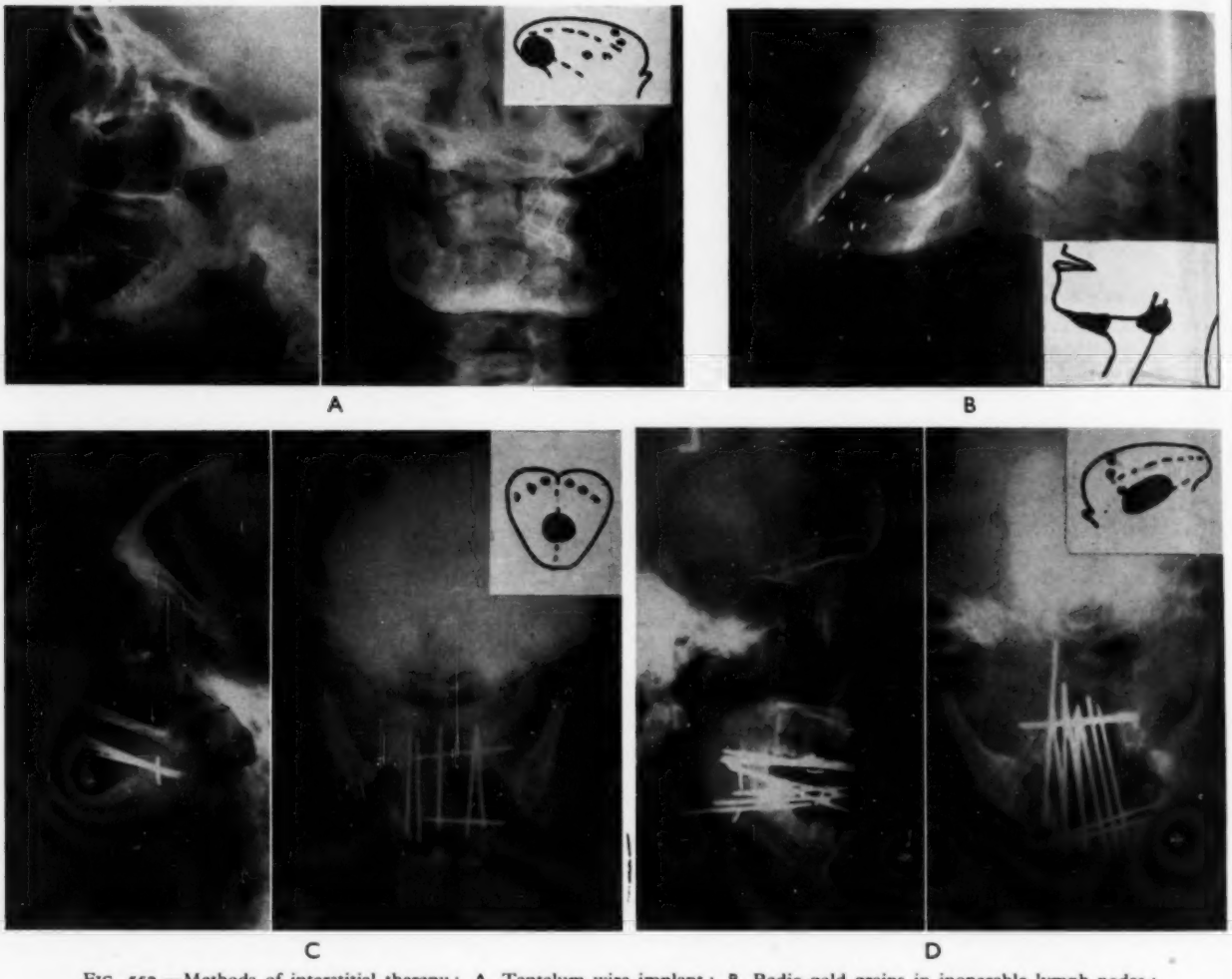


FIG. 552.—Methods of interstitial therapy: A, Tantalum wire implant; B, Radio-gold grains in inoperable lymph-nodes; C, Radium implant, single-plane; D, Radium implant, two-plane.

In 1938 experiments were undertaken (Wilson and Cade, 1938) in which implants that had been used in selected successful cases were reproduced in tongues obtained from cadavers. The dose at various representative points was measured with a Sievert chamber. The results suggested that the most satisfactory dosage rate lies between 30 and 60 r/hour, and that the dose should nowhere fall much below 5000 r, and may in places reach double this figure without harm. We have found that a dose of the order of 7000 r, or rather higher in small lesions, is desirable for best results.

1. Interstitial Radiumtherapy.—

Technique of Radium Implantation.—In the pre-operative phase attention is given to the teeth but no time is wasted. Extractions can be carried out at the time of the radium implant if necessary. The teeth adjacent to the implant are almost always removed, as well as any others which are in poor

is now unusual, but if it does occur the needle is at once replaced under general anæsthesia.

The surface extent of the lesion, its shape, and the volume of tissue to be treated are carefully assessed. The standard radium needles now available permit a considerable choice and afford flexibility in the planning of the implant. Most lesions can be adequately irradiated with a single plane implant; in bulkier tumours a volume implant is indicated (*Fig.* 552, C, D). The distribution of the needles is always checked by anteroposterior and lateral radiographs, and very occasionally an implant has to be corrected or even repeated. Such radiological control of the position of the needles is essential and forms a basis for dosage calculation. With a dose-rate of 40–50 r/hr. a total dose of 7000–8000 r can be achieved in seven days. Results are better and radiation effects more moderate if the overall period of treatment is about seven days than

if the same total dose is given in a shorter time. A combination of a radium implant for a reduced period followed by X-ray therapy, although practised in some centres, is to be deprecated and does not give the same clear-cut response to treatment. Intra-oral moulds have not been used for tongue lesions and the development of teletherapy has rendered this cumbersome method obsolete. The implantation and the whole period of the treatment are covered by antibiotics, usually penicillin and streptomycin by injection. Painstaking care is given to oral hygiene during the treatment, frequent cleansing by gentle mechanical irrigation with mild antiseptics being the most important method.

Selection of Cases.—We reject for interstitial therapy those cases which in our judgement will certainly fail to respond to radiation, or where an implant, to be adequate, would be too massive for the patient to tolerate. Fixed infiltrating growths (*Fig.* 553), involving a large proportion of the tongue and often associated with a positive Wassermann reaction, do not respond to radiotherapy. This also applies to cases showing much œdema of the tissues of the mouth floor, indicating lymphatic blockage, excessive fibrosis, and poor blood-supply. Such cases should not be implanted. If radiation is to be tried, it is better to use teletherapy. In many such cases, however, better palliation can be obtained with the diathermy. Growths extending on to the fauces are preferably treated by teletherapy and this sometimes applies to growths invading the mouth floor. Posterior-third lesions are difficult to implant accurately, and the patients suffer much discomfort. They, too, are usually more suitable for teletherapy.

Table V.—Operation Deaths

Case No.	Age	Procedure	Cause of Death
26/ 2	50	Terminal. Bled from fungating nodes	
27/ 1	54	Simultaneous implant and block of neck	Pneumonia
27/ 6	49	Diathermy to mouth floor	'Shock'
27/ 9	66	Lateral pharyngotomy	Pneumonia
27/13	60	Terminal	Œdema glottis
28/ 1	60	Simultaneous implant and block of neck	Secondary hæmorrhage
28/23	65	Posterior implant	Secondary hæmorrhage
29/ 1	73	Terminal. Implant	Delirium tremens
29/ 6	66	Block dissection neck	Pneumonia
29/49	63	Implant to neck	Septicæmia
30/16	66	Implant to neck	Pneumonia
30/25	62	Lateral pharyngotomy	Secondary hæmorrhage
31/ 2	73	Implants to double primary	Pneumonia
31/ 5	71	Neck implant	Pneumonia
31/13	68	Terminal. Implant	Delusional state
31/16	65	Implants to double primary	Pneumonia
31/20	66	Terminal. Implants to tongue and neck	Pneumonia
34/ 6	83	Implant	Pneumonia
36/ 2	50	Implant	Pneumonia
36/25	70	Implant	Pulmonary infarct
43/ 2	70	Terminal. Partial glossectomy	Pneumonia
49/10	65	Block dissection neck	'Shock'
49/31	81	Implant	Pneumonia
50/31	76	Implant	Pneumonia (?)
50/32	67	Implant	Pulmonary infarct
51/10	80	Terminal. Hemiglossectomy	Coronary block
52/17	73	Implant. Hopeless case	Pneumonia
53/24	60	Implant	Pneumonia
54/14	61	Implant	Coronary block
		Total 29	

Causes of Failure.—Failure of a radium implant may be due to bad technique, to bad selection, or to inherent radio-resistance in the tumour. The commonest technical mistakes are to make the implant too small in area or volume, and to misjudge the dose-rate. The ideal dose-rate is about 1000 gamma röntgen a day, and rates much higher than this should be avoided. They mean that the treatment must be terminated after four or five days and results are then much inferior. Longer-period implants, up to ten days, are satisfactory, but the needles are increasingly liable to come loose and the tax on the patient's morale is greater. Underdosage may be deliberate when the growth is very large or when the implant extends very close to the alveolus. It is usually a mistake, however, and we have come to accept the risk of a small area of necrosis, which will heal in time or may be treated surgically, rather than risk a recurrence from underdosage.

Fig. 553.—Fixed infiltrating carcinoma of almost the whole tongue unsuitable for radiotherapy.

As already stated, radio-resistance cannot always be predicted from the macroscopic appearance of the tumour. Because of this we still have to accept a certain number of radiation failures, the lesions either failing to heal or showing signs of recurrence within a few months. What we have learned over the years is to recognize these failures as soon as possible and treat them by prompt surgery. Sometimes, if the failure is only partial or local, supplementary diathermy is sufficient. In other cases radical surgery is required. Repeated implants are no longer practised.

Mortality and Morbidity.—Twenty-nine of our 653 cases have died in hospital during or after treatment. The deaths are set out in *Table V*. Fifteen of them followed radium implants to the tongue. The majority of them were in the early days and usually from bronchopneumonia. Since the war there have only been 6 deaths from radium implantation.

We have carried out a total of 573 tongue implants in 507 cases, so that the true mortality is 15 in 573 operations, or about 2·6 per cent. This, it must be repeated, includes many terminal cases which would have been quite unsuitable for surgical resection.

The morbidity of radium implantation is more difficult to express in figures. It varies from slight persistent soreness of the tongue or dryness of the mouth to a radium necrosis which may be confined to soft tissues or may involve bone. As mentioned above, we have come to accept minor degrees of necrosis as a reasonable risk and in our records necrosis is mentioned in 33 cases. The great majority of these healed spontaneously, but a few required diathermy excision and a very few major surgery such as partial removal of the mandible. In the latter cases radiation damage was often complicated by persistence of the lesion, which was usually an advanced one.

2. Teletherapy.—Conventional X rays of the 200–400 kilovolt range have proved disappointing in the treatment of tongue cancer, both in our experience and in the literature. Where external radiation is indicated for tongue carcinoma it should be given either by supervoltage X rays, i.e., 2 million volts or more, or gamma rays. Our main experience has been with teleradium units, commencing in 1929 with 1 gramme, gradually increasing in size to 10 grammes and more recently replaced by radio-cobalt up to the amount of 30 curies, the Van de Graaff 2-million-volt generator, and the Theratron containing 2000 curies of cobalt in a rotating unit. We have no personal experience of the treatment of these cases with the linear accelerator or other sources of supervoltage rays, which now range up to 50 million electron volts. Rotation therapy is a technique the value of which for this lesion is as yet undetermined, but it appears to have attractive advantages.

In some centres, notably the Radiumhemmet, Stockholm, teletherapy is considered the method of choice in most cases. In our view, however, it has certain serious drawbacks which must be taken into account. Firstly, the treatment time is prolonged, usually six weeks or more, and secondly the amount of healthy tissue which has to be irradiated may be very great. The resulting dryness of the mouth and other discomforts can be very distressing to the patient and result in marked loss of health and weight. Because of the larger volume of tissue treated, the dosage rate has to be much slower than with implantation, where a total of even 8000 r or more can sometimes be given in a week. For these reasons we feel that teletherapy should not be the method of choice for all tongue lesions, but only for those inaccessible to accurate implantation, or where the growth is very large, or where slow treatment is an advantage. In the latter group we include, as already stated, large ulcerated lesions, especially if involving adjacent structures, those involving bone, and those with much sepsis and œdema. Attempts to implant the posterior third of the tongue have been made by various methods: by lateral pharyngotomy in the early days, by the 'tongue-pterygoid implant' of Ralston Paterson, and in more recent times by using curved cobalt needles or by implanting through the suprahyoid skin. Radon seeds (removable and non-removable) and radio-active gold grains have also been used. On the whole these methods have proved unsatisfactory and teletherapy is to be preferred. It has, moreover, the advantage that the upper deep cervical areas are automatically included in the fields of treatment. For palliative purposes, particularly in very extensive growths, teletherapy, given gently, has advantages over implantation.

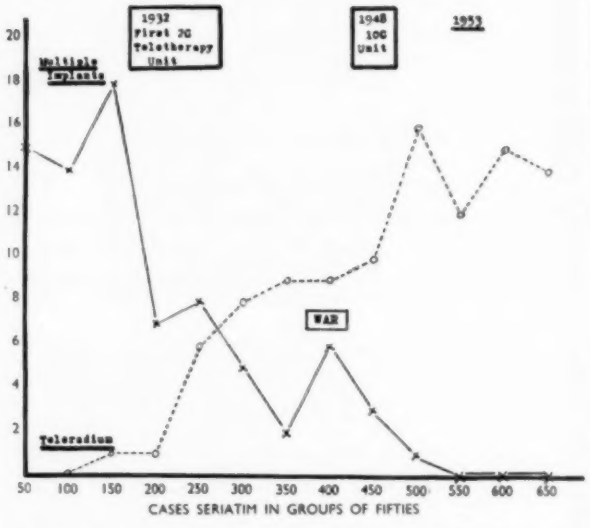


FIG. 554.—Chart showing the change in trends in radiotherapy to the tongue, 1925–55.

Since radio-active cobalt became available for clinical use, teletherapy has rapidly widened its scope. The limitations inherent in the use of relatively small quantities of radium, between 2–10 grammes, were gradually overcome when units containing 15–50 curies of cobalt came into use. Further rapid progress was made when apparatus containing 1500–2000 curies of cobalt, such as the Theratron, became available. The great clinical advantages of such powerful sources of gamma rays in the treatment of cancer of the posterior or pharyngeal portion of the tongue, unsuitable for needling, can be summarized as follows: (1) Less injury to the skin as the maximum dose is received deep to the skin surface. (2) Less incidence of bone necrosis of the jaws owing to a nearer approximation of the energy absorption of soft tissue and bone. (3) Less severe mucosal reactions from a more precise limitation of the irradiated field and a more accurate beam direction. The great disadvantage of teleradium remains the overall period of treatment which varies from six to eight weeks. The graph in *Fig.* 554 shows the increasing use we have made of teletherapy over the years.

3. Surgery.—The enormously increased facilities now available to the surgeon have not unnaturally led to a re-trial, particularly in the United States, of radical surgery in cancer of the tongue. The most obvious changes are the advances in anæsthetic techniques and the use of antibiotics and extensive blood transfusion. There is no doubt that very wide ablations can now be carried out with negligible mortality. In some cases, however, satisfactory

clearance can only be obtained at the cost of great mutilation and in other cases, particularly those of the posterior third of the tongue or those involving the fauces, the clearance can never be said to be satisfactory. Moreover, the patients are not suited to elaborate multi-staged procedures, without which satisfactory closure of mouth wounds is sometimes difficult. One feels that in the enthusiasm for surgery the patient's personal viewpoint has sometimes been disregarded: though cured, he may find himself so disabled as to be incapable of earning a living, and so mutilated as to be socially unacceptable.

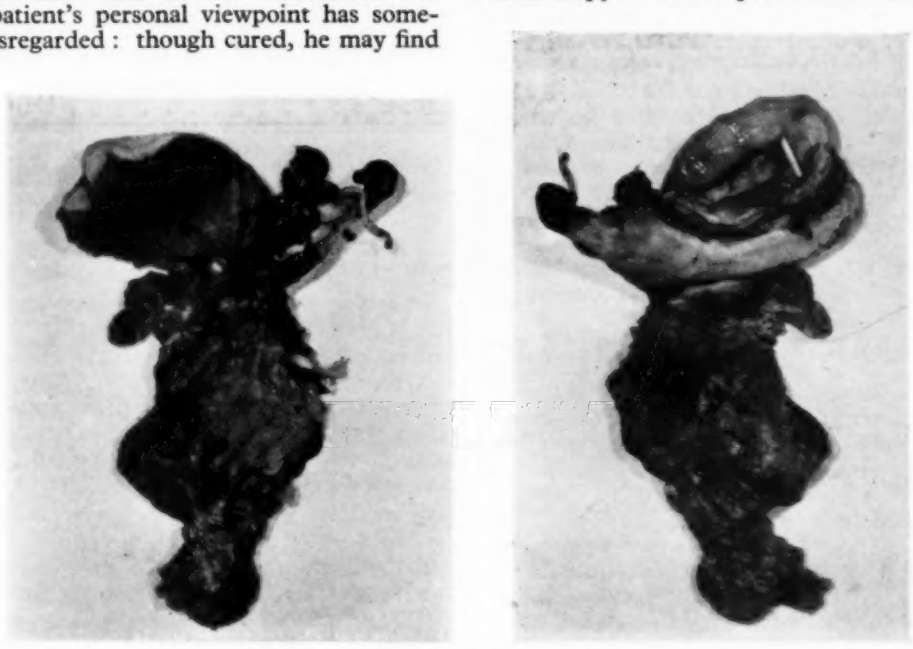


FIG. 555.—Specimen of carcinoma of the tongue removed by radical operation, showing right half of the tongue, mouth floor, and mandible, and right cervical nodes with sternomastoid muscle and internal jugular vein.

In our opinion the indications for radical surgery are few and include primary radio-resistance of tumours and post-radiation recurrences. Repeated implantation has now been abandoned as too dangerous (*Fig.* 554) and we tend to resort more rapidly to surgery where irradiation proves unsatisfactory. In such cases partial glossectomy with the diathermy needle is the usual method. Invasion of bone by a tumour was formerly thought to be a clear indication for surgery, but the position is now less certain. External megavoltage radiation has proved successful in these cases in recent times, helped by the control of sepsis with antibiotics. Reports from other centres confirm that the involvement of bone is no longer a firm contra-indication to external radiation. Syphilitic glossitis may exceptionally be an indication for surgery.

Palliative excision or coagulation by diathermy is a useful method in some lesions which are beyond the range of excisional surgery and where sepsis and cellular infiltration of connective tissue may be controlled and reduced. This is a method much favoured at the Radiumhemmet, and we have come to resort to it more and more promptly in cases not responding fully to irradiation.

Radical Surgery.—In a small group of cases the method of choice is wide surgical excision which includes half the lower jaw, half the tongue, and mouth floor. This usually is combined with a radical block dissection of the neck including the posterior belly of the digastric (*Fig.* 555). The indications for such a procedure are extensive lesions involving the undersurface of the tongue and the gingival mucosa. Most patients have had previous radiotherapy and have proved resistant to radiation. With the advent of megavoltage therapy and the use of large cobalt units, primary healing following operation is not delayed by the previous radiation. Experience with this procedure has led to certain minor modifications in technique which have lessened post-operative morbidity. Disarticulation at the temporomandibular joint is always to be preferred to transection of the mandibular vertical ramus. The cut surface of the tongue should not be sutured to the buccal mucosa as this results in considerable speech defect; the cut intrinsic muscles of the tongue are left free and become covered by epithelium within a few weeks. This leaves a more mobile half tongue and speech is nearly normal. Bone-grafting to replace the lost half mandible is not always needed, the resulting deformity being small as long as only half the mandible is removed (*Fig.* 556). With a

FIG. 556.—Patient after hemiresection of the mandible and partial glossectomy to show good function.

mobile half tongue a dental plate can satisfactorily restore the contour of the lower half of the face. Grafting is however needed if the whole chin is included in the resection or if the entire mandible is excised.

The Cervical Lymph-nodes.—Our policy throughout the whole series reported has been to advise surgery in preference to radiotherapy in all those cases deemed suitable. This conforms with the opinion of almost all workers that surgery gives the best results in the case of the cervical lymph-nodes. Our preference has been for the full block dissection of Crile, including removal of the internal jugular vein, the sternomastoid muscle, and the posterior belly of the digastric. Partial dissections, such as submandibular clearance, though frequent in the early days, are now seldom resorted to unless as part of an operation for removal of a primary tumour. *Table VI* surveys the treatment of the nodes of the 5-year cases. The total number of

Table VI.—Treatment of Cervical Lymph-nodes, 1925–50 (518 *Cases*)

1. No treatment :—		
a. No nodes	48	
b. Nodes, but treatment not worth while	75	
Total		123 (24 per cent)
2. Surgery :—		
a. Block dissection	81	
b. Partial dissection	44	
Total		125 (30 per cent)
3. Teletherapy as main treatment		154 (35 per cent)
4. Radium (mostly supplementary treatments)* :—		
a. Moulds and plaques†	91	
b. Implants	99	
Total		190 (38 per cent)

* Many cases in Group 4 had already received treatment by one of the other methods.

† This method seldom used after 1939.

patients treated by full block dissections was 117 out of 653, including 8 bilateral dissections. In addition, partial dissections were carried out in 47 cases. Since the end of 1950 there have been 35 full, and only 2 partial, dissections.

It is pertinent to ask, if block dissection is the best treatment, why it has been carried out on only 1 in 6 of our cases (*Table VII*). The reason lies partly in the strictness of our criteria, which are as follows :—

1. The primary lesion must be healed, or at least controlled. For this reason we feel that neck dissection should not as a rule be carried out within three weeks or so of the radium implant. Failure to observe this rule has led in one or two cases to widespread malignant infiltration of the tissue planes of the neck.

2. The nodes must be operable. Where they are very large, or where the skin is extensively infiltrated, or where there is deep fixation to the carotid sheath, rapid recurrence after surgery is common, and radiotherapy is usually a better choice.

3. Nodes must be palpable. Prophylactic dissection has been carried out by us in only 3 cases. This rule presupposes, of course, that follow-up observation is strict and regular, and that whenever a node is discovered, operation is undertaken at once.

A critical review of these indications, particularly the last, is appropriate. Our objections to prophylactic dissection are as follows: (1) Nodes may never appear; (2) The primary lesion may persist or recur, and pass out of control; (3) Node involvement, if it does occur, may prove to be contralateral (*Fig.* 557). Support for our attitude comes from Hayes Martin (1951), who has produced convincing statistical evidence in a large series of cases that for one prophylactic operation that might be of benefit, four useless operations would be carried out. In almost all centres opinion is against prophylactic dissection, but Tailheffer (1952) in Paris is in notable disagreement. He believes in and practises the prophylactic operation in all suitable cases.

Table VII.—Block Dissection of Cervical Nodes: Frequency, 1925–55

Period	Total Number of Cases	Number Treated by Block Dissection	Percentage
1925–50	518	82	16
1951–55	135	35 + *	26
1925–55	653	117	17·6

Number of bilateral dissections (complete), 8.

* Further recent cases may yet require block dissection.

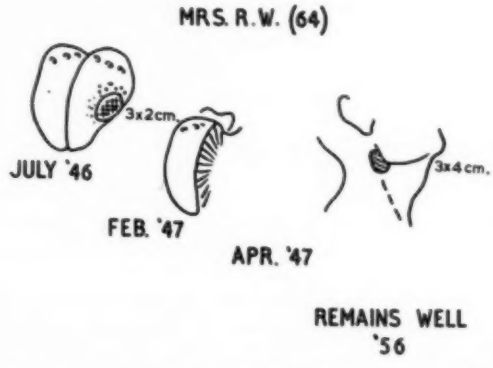


Fig. 557.—Case showing node involvement on the opposite side only; the left-sided tongue primary was treated by a radium implant and subsequently by diathermy excision of an active residue. Lymph-nodes appearing on the opposite side of the neck were removed by block dissection and histologically confirmed. Patient remains well 9 years later.

We have found it instructive to review our own material. In *Table VIII* an attempt has been made to analyse the reasons for withholding block dissection in 437 out of 518 cases. In 284 there were obvious contra-indications: the primary disease was uncontrolled, the nodes were inoperable, or the patient was unfit. These were cases which, on critical review, it seems could not have been saved by surgery at any stage. In a further 89 cases no nodes ever appeared, and therefore dissection was not considered necessary. In 10 cases the records are obscure; the patient died during treatment or

was lost to follow-up at an early stage. There remain about 50 cases where the outcome *might* have been influenced by a prophylactic dissection or possibly a combined operation at the initial treatment. They include cases where the nodes were of borderline operability at the first attendance; where difficulties in treating the primary occasioned delay; or where the follow-up attendance of the patient was unsatisfactory. This last marginal group—10 per cent or less of cases—represents the outside limit of the gain

Table VIII.—Analysis of Reasons for Withholding Block Dissection
(437 5-*year Cases*)

Group I. Indeterminate :— Records obscure; died during treatment of primary; lost to follow-up at early stage	14 (3 per cent)
Group II. Block deemed unnecessary :— Cases without nodes	89 (20 per cent)
Group III. Block contra-indicated :— Primary disease uncontrolled; nodes inoperable; patient unfit	
These cases, it appears on critical review, could not have been saved by surgery at any stage	284 (65 per cent)
Group IV. Missed opportunity? :— *Might* have been saved either by earlier, perhaps prophylactic block, or combined operation at the start. It is a hypothetic optimal figure	50 (11 per cent)

which could follow a policy of prophylactic dissection. Against it must be set the many needless or useless operations which would be carried out.

The problem has been approached in another way in *Table IX*. Here the value of the block dissections carried out by us is weighed in each case in the light of the subsequent history of the patient.

Table IX.—Assessment of Results of Block Dissection of Nodes
1925–50

Total cases treated by block dissection		81
Indeterminate :—		
Lost, or died of intercurrent disease	3	
*Hodgkin's disease	1	5
*Lymphosarcoma	1	
Determinate cases		76
1. *Operation justified by outcome* :— No recurrence in operation site, and survived at least a year without primary recurrence		31
2. *Probably justified* :—		
a. No recurrence in primary or operation site, but died of disease within a year or so		10
b. Recurrence in operation site, but only after some years		
3. *Not justified* :—		
a. Local recurrence in operation site	16	
b. Early and fatal primary recurrence	15	35
c. Operation deaths	4	
Total		76

* Histological Diagnosis, made post-operatively.

If the patient survived at least a year without recurrence of the primary growth, and if there was no recurrence in the operation area in the neck, we consider that the operation was justified. On the other hand, operative deaths must be counted as failures; while early recurrence in the operation area and early uncontrolled primary recurrence means that the operation was in vain. On this basis it appears that about half the operations were justified in the event. Could this figure be improved by prophylactic dissection? Tailheffer maintains that it can be and is.

The probable conclusion of the matter is that neither a rigid policy of withholding nor of practising block dissection is ideal. Each case should be considered on its individual merits, in an endeavour to select those few which in fact demand prophylactic dissection. Where the primary lesion is very small and slow-growing, and of well-differentiated histological type, and where the patient is reliable, careful observation alone is probably enough. Where the lesion is moderately large but responds well to treatment, and particularly if it is well away from the midline, prophylactic dissection might show handsome dividends. Where, however, the lesion is very extensive, or anaplastic in type, or near the midline, it is probably better cautiously to await events: block dissection may be made unnecessary by the march of the disease. This also applies where there is extensive leucoplakia and multicentric growths are a possibility. Our present attitude may be summed up by saying that we believe prophylactic dissection to be called for very seldom; but we are prepared to carry it out in a small selected group of cases.

Radiotherapy in the Management of Cervical Nodes.—

1. *Indications.*—In the following groups of cases we consider radiotherapy to be the method of choice for the cervical nodes :—

a. Where the histology of the lymph-nodes removed at block dissection is positive, post-operative radiation is advisable.

b. In posterior-third lesions treated by external radiation the upper deep cervical nodes are necessarily included in the treatment fields. In our series of lesions involving the posterior third of the tongue, 85 per cent had clinically malignant nodes when first seen. Block dissection is very rarely indicated in these posterior-third cases.

c. Inoperable lymph-nodes must necessarily be treated by radiation, and the only problem is the choice of method.

d. There are in addition certain cases to be judged individually where the primary disease is uncontrolled, or the glands are bilaterally enlarged, or the patient is ill or feeble, where radiotherapy may be judged superior to surgery.

2. *Methods.*—

The following techniques are available :—

a. External radiation : In our series this has been mainly given by teleradium. The sizes of fields and the percentage depth dose of the beams are eminently suited to this particular situation. Teletherapy has been used as a post-operative supplement, as indicated above, and in the treatment of glands considered inoperable by reason of deep fixation or skin ulceration rather than widespread involvement. The method is less suitable for complete irradiation of the whole neck to full tumour dose, though this may sometimes be accomplished satisfactorily with great attention to technical detail. In selected cases it is

possible to irradiate quite bulky glandular masses up to a dose of 5000–6000 r in five or six weeks, without producing moist desquamation of the skin or serious damage to deep structures.

b. Interstitial methods: Implantation may be 'closed' or 'open'. The former is the routine method and may be applied to the whole neck. For this purpose a rectangular single-plane implant is built up along the whole length of the sternomastoid muscle, and its lower part is extended backwards to include the supraclavicular glands. The needles are thrust deeply into the sternomastoid muscle from before backwards. At the upper end a forward extension is made to take in the submandibular and submental glands. Such an implant is shown in *Fig.* 558. The dose may be taken to 6000 r in seven days and we can record some lasting cures by this method. Its chief disadvantage is the intense fibrosis occasionally caused.

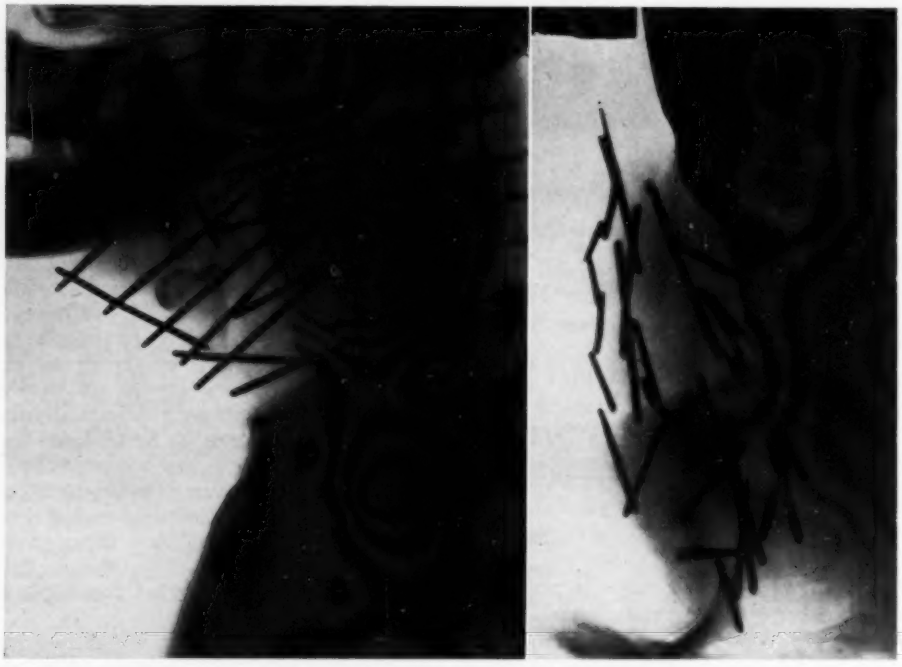


FIG. 558.—Radium implant to inoperable cervical lymph-nodes. The part of the implant related to the main mass is in two planes, the remainder is in a single plane.

Open implantation is of value when the skin has already been damaged by radiotherapy, and it also gives greater accuracy of implantation in some difficult areas, notably the supraclavicular fossa. In this method the skin-flaps are dissected back and the needles inserted direct into the tumour area. The wound is loosely sutured and a week later reopened for the removal of the needles. Healing is usually satisfactory.

Implantation with radon seeds or radio-active gold 'grains' is useful, particularly for palliative purposes. It may be of value in patients who are too old or feeble for more radical procedures, in very advanced cases, or in cases with recurrence after surgery. It may also be used where persistence of the primary tumour renders more radical treatment of the lymph-nodes unsuitable, and as a supplement to other methods of treatment.

III. RESULTS

In assessing our results we have conformed to the usual practice and adopted the 5-year survival as a convenient yardstick. We have accepted Hayes Martin's conception (1951) of determinate and indeterminate cases for the purpose of calculation, and have accordingly excluded the following cases:—

1. Patients dying of intercurrent disease during the 5-year period clinically free from carcinoma.

2. Patients lost to follow-up within the 5-year period. Operative deaths, which have been counted as failures, number 29, as set out in *Table V*.

The overall 5-year survival rates are recorded in *Table X*, but analysis of these figures shows that they conceal some widely differing components.

Table X.—RESULTS OF TREATMENT (*5-year Survival Rate*)

Total cases treated up to end of 1950		518
Indeterminate:—		
Died free from disease within 5 yr.	18	
Trace lost within 5 yr.	37	
Died before treatment started	2	
TOTAL		57
Determinate cases		461
Cases survived at least 5 years		124
Percentage of determinate cases	27	
Percentage of total cases	24	

N.B.—Operation deaths (25) are included as failures.

Some discussion of factors affecting the prognosis is therefore of interest:—

1. *Stage of the disease*: The very marked influence of the size of the primary lesion and the state of the lymph-nodes is shown in *Table XI*. It will

be seen that both factors are of roughly equal importance.

2. *Site*: The site of the disease has a supremely important bearing on prognosis, as shown in *Table XI*. As already mentioned, 85 per cent of the patients with posterior-third lesions have glands already present at the commencement of treatment.

Lesions which cross the midline have also been considered separately. It will be seen that the 5-year prognosis (16 per cent) is materially worse than

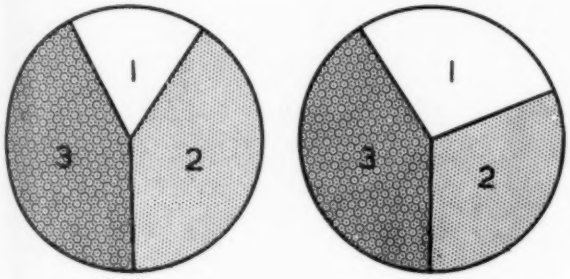


FIG. 559.—Diagram showing the proportion of small lesions (1), large lesions (2), and lesions extending beyond the tongue (3), for men and women respectively. In women the percentage of small lesions is significantly greater.

the overall figure of 27 per cent. The difference is probably due, however, to the smaller number of 'small' lesions—8 per cent against 18 per cent in the whole series.

It thus becomes clear that the really poor results are in posterior-third growths, which are almost

Table XI.—RESULTS OF TREATMENT—(*continued*)

(*Figures give Percentages of Determinate Cases*)

5-year Prognosis according to Stage of Primary Lesion

Overall 5-year survival rate		27 per cent
Lesions confined to tongue	35 per cent	
Less than 2 cm. diameter	60 per cent	
More than 2 cm.	23 per cent	
Lesions not confined to tongue	16 per cent	

Five-year Prognosis according to Lymph-node Involvement

Overall 5-year survival rate		27 per cent
No nodes when first seen	51 per cent	
No nodes at any time	78 per cent	
Nodes developed	30 per cent	
Nodes when first seen	14 per cent	

Five-year Prognosis according to Site

Overall 5-year survival rate		27 per cent
Lesions confined to anterior two-thirds	35 per cent	
Involving posterior-third	11 per cent	

Growths Transgressing the Midline

Total cases	143
Determinate	125
5-year survivals	20
Percentage	16

never amenable to surgery and are ill-suited to interstitial therapy. It is still too early to perceive whether the new supervoltage equipment now available will materially improve these results. By contrast, growths confined to the anterior two-thirds of the tongue, and particularly small lesions and those without lymph-nodes, show relatively satisfactory results.

Effect of Sex on Prognosis.—*Table XII* shows that the 5-year survival rates are apparently much higher in women than in men. The difference—39 per cent against 24 per cent—is three times the standard error and is therefore statistically significant. If, however, the material is broken down into stages of the disease (*Fig.* 559) it is found that this apparent difference is satisfactorily accounted for by the

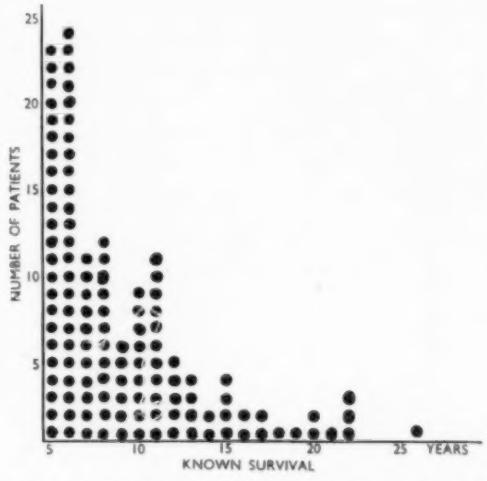


FIG. 560.—Diagram showing the numbers of patients surviving 5 to 26 years after treatment.

earlier stage at which women on the average report for treatment. Our clinical impression indeed, though the cases are few, is that in young women at any rate the disease is more rather than less difficult to cure.

Table XII.—EFFECT OF SEX ON FIVE-YEAR SURVIVAL RATE

	Male	*Female*	*All*
Total cases to end of 1950	415	103	518
Determinate	369	92	461
5-year survivals	88	36	124
Percentage of 5-year survivals	24*	39*	27

* This difference is three times the standard error and therefore statistically significant.

Long-term Results.—*Fig.* 560 lists the patients surviving more than 5 years and *Table XIII* shows the ultimate fate of all these patients. Only about one-sixth of them are known to have died of disease; but in a further 20 per cent we have lost touch with the patients and have been unable to trace records of their deaths at the General Register Office. Forty-eight patients survived for periods between 10 and

Table XIII.—FIVE-YEAR SURVIVORS (124 to end of 1950)

Fate of Patients

Remain alive (1956)	39 (31·5 per cent)
Died of intercurrent disease*	39 (31·5 per cent)
Lost, but no record of death at R.-G.'s office	24 (19 per cent)
Died of disease	22 (18 per cent)

* 8 died of a second independent cancer, viz.: breast (2), œsophagus, bladder, 'eye', lung, rectum, lymphadenoma.

26 years after treatment, and 39 patients died of old age or intercurrent disease, free from carcinoma. *Table XIV* reviews these cases in more detail.

Late Recurrences.—Reactivation of disease may occur locally after many years of apparent 'cure' (*Table XV*). The late local recurrences in our series number 13 patients; in 7 of these the predisposing factor of leucoplakia was present. Late recurrence following radiotherapy as long as 21 years after treatment has been recorded by Dr. Juliette Baud.

Table XIV.—Patients Surviving more than Five Years

Known Survival in Years	Subsequent Fate				Total
	Lost Trace	Died of Disease	Died Free from Disease	Living	
5	2	6	9	6	23
6	4	3	8	9	24
7	5	3	1	2	11
8	3	2	3	4	12
9	2		3	1	6
10	1	1	3	4	9
11	2	1	3	5	11
12	1	2	1	1	5
13	2		2		4
14			1	1	2
15			3	1	4
16				2	2
17	1		1		2
18		1			1
19			1		1
20				2	2
21			1		1
22	1	1	1		3
26	1				1
	25	20	41	38	124

Table XV.—Late Local Recurrence

Years after Treatment	*Number*
5	5
6	1
8	3
10	3
16	1
Total	13

Palliative Results.—We think it is worth while to emphasize the great palliative value of the radium implant. Whatever the ultimate fate of the patient, healing of the primary growth gives tremendous symptomatic relief. *Table XVI* attempts to assess this palliative value. It shows the percentage of lesions satisfactorily healed by a radium implant for at least a year or so, though not necessarily permanently. The figures can only be approximate because the records are sometimes obscure in the older cases. In a few instances diathermy excision of doubtful residues followed the main (interstitial) treatment. The prospect of healing is surprisingly good even in advanced cases, while small lesions may be expected to heal in nine cases out of ten.

Table XVI.—Palliative Value of Interstitial Therapy Expectation of Primary Healing

Type of Case	*Percentage Induced to Heal*
Small primary (94 cases)	95
Large primary (157 cases)	64
Primary extending beyond tongue (147 cases)	48
Multiple, recurrent, and unclassified (3) (58 cases)	53
Total (456 cases)	64

Note: Up to the end of 1954, 478 cases were treated by implantation of the primary growth. Twenty-two must be discarded, leaving 456 determinate cases. Operative deaths counted as failures.

CONCLUSION

In a disease such as carcinoma of the tongue, when the results of any form of treatment leave so much to be desired, it is to be expected that the pendulum will swing between one form of therapy and another. In our view the swing of the pendulum away from radical surgery which followed the introduction of radium techniques has been well justified.

It is clear from the study of our series of patients that interstitial radium has much to recommend it in suitable cases. This method makes possible the delivery of an adequate dose of radiation within a very short period of time, in most cases one week. The post-radiation effects are moderate and subside in about three to four weeks. Scarring is minimal and the functional result good. Primarily radioresistant lesions can be recognized early and submitted to surgery without dealy. Teletherapy is the method of choice in lesions of the posterior part of the tongue, in large tumours, and in cases deemed unsuitable for needling. Palliative and radical surgery are reserved for selected cases. The treatment of choice for cervical lymph-nodes remains radical or block dissection of the neck under certain well-defined conditions. Taking into account the great palliative value, we feel that radiumtherapy remains the method of choice in the great majority of patients.

Acknowledgements.—The authors wish to express their gratitude to Dr. C. W. Wilson, head of the Department of Physics at Westminster Hospital, for his valued assistance so readily given through the years. They also wish to thank Dr. Peter Hansell, head of the Department of Medical Photography, Westminster Hospital, for his help with the illustrations for this paper.

REFERENCES

Baud, Juliette (1950), *Amer. J. Roentgenol.*, **63**, 701.
Cade, Sir S. (1953), *Brit. J. Surg.*, **41**, 225.
Evans, A., and Cade, S. (1927), *Ibid.*, **15**, 55.
Gibbel, M. I., Cross, J. H., and Ariel, I. M. (1949), *Cancer*, **2**, 411.
Jacobsson, F. (1948), *Acta radiol., Stockh.*, suppl. 68.
Martin, H. (1951), *Cancer*, **4**, 92.
Paterson, R. (1948), *The Treatment of Malignant Disease by Radium and X-rays*. London: Arnold & Co.
— — and Parker, H. M. (1938), *Brit. J. Radiol.*, **11**, 252 and 313.
Registrar-General's Annual Statistical Review (1920-53). London: H.M. Stationery Office.
Tailheffer, A. (1952), *Proc. R. Soc. Med.*, **45**, 758.
Waldenström, J., and Kjellberg, S. R. (1939), *Acta radiol., Stockh.*, **20**, 618.
Wilson, C. W., and Cade, S. (1938), *Brit. J. Radiol.*, **11**, 599.

CHOLECYSTITIS GLANDULARIS PROLIFERANS

By L. P. LE QUESNE and I. RANGER

FROM THE DEPARTMENT OF SURGICAL STUDIES AND BLAND SUTTON INSTITUTE, THE MIDDLESEX HOSPITAL, LONDON

THE development of epithelial sinuses, or diverticula, penetrating into, or even beyond, the muscle coat is a common and well-recognized change in chronic cholecystitis. These diverticula are often referred to as Rokitansky-Aschoff sinuses, a name which in the past has led to much confusion. In 1842 they were clearly and correctly described by Rokitansky as 'hernia-like out-pouchings of the gall-bladder mucosa'. Unfortunately, in 1905, Aschoff referred to these same structures as 'Luschka ducts', confusing them with the minute, aberrant bile-ducts described by Luschka in 1858 and 1863. To make the confusion worse Shikinami (1908) referred to these epithelial out-pouchings as 'Aschoff ducts'. This whole subject is fully discussed by Halpert (1927), who clearly shows that there are two distinct, different structures: (*a*) Luschka's ducts, which "are duct-like structures found occasionally in the periphery of the gall-bladder wall, occurring most frequently on the hepatic surface of the viscus and usually along the edges of the fossa vesicæ felleæ. They have a wall of their own with the histological structure of the intrahepatic bile-ducts". (*b*) Rokitansky-Aschoff sinuses, which "are deeper out-pouchings or sinuses of the gall-bladder mucosa, which dip down into the muscularis or extend as finger-like processes through the muscular coat into the perimuscular layer".

These mucosal out-pouchings or Rokitansky-Aschoff sinuses were carefully investigated by Robertson and Ferguson (1945), who examined 320 surgical specimens and 175 gall-bladders obtained at autopsy. They concluded that in approximately 50 per cent of normal gall-bladders there are invaginations of the mucosa, reaching sometimes as far as the serosa. They pointed out that these mucosal invaginations tend to branch, and that though originally connected to the lumen of the gall-bladder by narrow tortuous channels, this connexion may become obstructed, leading to the formation of small cysts. In cases of chronic cholecystitis they found that these mucosal diverticula were more common and tended to penetrate more deeply than in the normal, and they described various complications of these diverticula, such as stone and abscess formation. These same authors also described how localized collections of such diverticula or cysts may form a macroscopic nodule in the gall-bladder wall, sometimes referred to as an 'adenoma'.

This gross form of the disease has been given a bewildering variety of names, King and MacCallum (1931) listing no less than ten different titles found in the literature. In their valuable paper, based on an examination of 25 well-marked examples, King and MacCallum describe the changes in detail, and show conclusively that the essential lesion is an excessive formation of epithelial sinuses (Rokitansky-Aschoff sinuses), many of them penetrating the muscularis, with associated chronic inflammatory changes and muscular hypertrophy. They suggested that the condition should be known as cholecystitis glandularis proliferans, a title which has gained fairly general acceptance, though in radiological journals the condition is often referred to as diverticulosis of the gall-bladder. Recently 12 cases of the condition, illustrating most of its main features, have come to our notice.

CASE REPORTS

Case 1.—Male, aged 40 years. Eighteen-months' history of pain between the shoulder-blades radiating through to the epigastrium, usually coming on 2-3 hours after food. No significant clinical signs. Barium meal: Some deformity of duodenal cap, but no crater or tenderness.

FIG. 561.—*Case* 1. Cholecystogram, showing the smooth, rounded filling defect at the fundus.

CHOLECYSTOGRAM (Dec. 1, 1953).—The gall-bladder functions normally. There is some suggestion of a smooth filling defect in the fundus which may be an 'adenoma'. Repeat Jan. 7, 1954. Examination confirms the presence of a smooth rounded filling defect in the fundus (*Fig.* 561).

OPERATION (Feb. 5, L. P. LeQ.).—Soft tumour, ¾ in. diameter, palpable in fundus of gall-bladder. Cholecystectomy performed: has been symptom-free since operation.

THE GALL-BLADDER (9 × 3·5 cm., *Fig.* 562).—Externally the gall-bladder appeared normal save that over the fundus the wall was rather opaque: at this point a soft, circumscribed tumour was palpable. Macroscopical section showed a white, partially cystic tumour, with a well-marked dimple in its mucosal surface, though the mucosa itself appeared normal: most of the cysts could be seen to lie outside the muscle coat, but the overlying serosa appeared normal. The remainder of the gall-bladder appeared normal. The orifice of the cystic duct was very small (2–3 mm.), but beyond this apparent diaphragm stricture the duct was normal. No stones present in the gall-bladder.

Histology.—Sections from the body of the gall-bladder show no gross histological abnormality. The mucosa is lined by tall, columnar epithelium, with some superficial epithelial sinus formation, not extending into or through the muscularis (*Fig*. 563). Little chronic inflammatory-cell infiltration is seen, and the muscle is of normal thickness. The fundal nodule, which is clearly demarcated from the normal wall, consists of epithelial sinus formation, with muscular hypertrophy. Many of the sinuses penetrate through the thickened muscularis, beyond which they terminate either in cystic dilatations, or by dividing into multiple branches. Some of the sinuses on the inside of the muscle coat project into the lumen, forming frond-like polyps (*Fig*. 564). In the perimuscular layer there is chronic inflammatory-cell infiltration and fibrosis, which extends to surround some of the muscle-fibres. Throughout the fundal area the sinuses are lined by tall columnar epithelium, with distinct mucus-cell formation in some of the deeper protrusions (*Fig*. 565). Muscular hypertrophy is pronounced, with hypertrophy of the smooth muscle of the blood-vessels. The serosa is intact over the fundal nodule.

FIG. 562.—*Case* 1. Photograph of the excised gall-bladder. The white, partially cystic, fundal nodule is clearly seen, with its central pit. The remainder of the gall-bladder is normal.

FIG. 563.—*Case* 1. Section from the body of the gall-bladder. The muscularis is of normal thickness and there is some superficial epithelial sinus formation, as is commonly present in any normal gall-bladder. (× 42·5.)

FIG. 564.—*Case* 1. Section from the fundal nodule. Epithelial sinus formation is present. On the mucosal aspect many of these sinuses project to form frond-like polyps. Others penetrate the greatly thickened, hypertrophic muscularis, beyond which they can be seen branching and forming cyst-like spaces. Chronic inflammatory changes are present in the subserosal (perimuscular) layer. (× 12.)

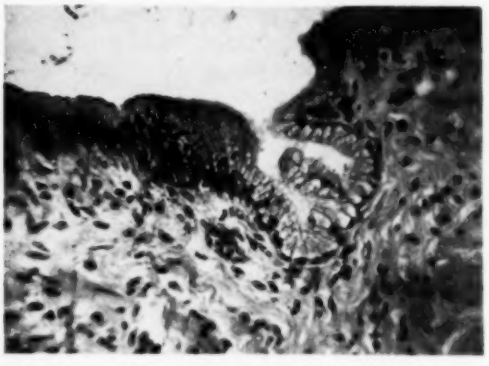


FIG. 565.—*Case* 1. Section from the fundal nodule, under higher magnification. An area of mucus-cell formation is shown, with tall, columnar epithelium on either side. (× 165.)

Case 2.—Male, aged 57 years. Autopsy specimen: death from carcinoma of stomach: no history of symptoms referable to gall-bladder.

THE GALL-BLADDER (11 × 3 cm.).—Externally there was a slight, rather opaque protrusion at the fundus, but otherwise the viscus appeared normal. On opening, a cystic mass, 1·5 cm. across, was seen at the fundus, with a well-marked central pit. The cystic spaces contained small pigmented calculi, but there were no stones in the gall-bladder itself. The mucosa and serosa covering the fundal mass were normal in appearance, as was the remainder of the gall-bladder.

Histology.—The whole organ showed increased subserous fibrosis, presumably resulting from previous gastric operations. The muscularis and mucosa of the body of the gall-bladder were normal, with slight, superficial epithelial sinus formation. At the fundus there was epithelial sinus formation, extending through the hypertrophied muscularis, with chronic inflammatory changes. Some of the extramuscular cystic spaces contained calculous debris.

Case 3.—Male, aged 63 years. Autopsy case: death from carcinoma of the intrahepatic bile-ducts.

THE GALL-BLADDER (9 × 4 cm.).—Externally the gall-bladder appeared rather opaque, particularly at the fundus, where a distinct intramural nodule, 1 cm. in diameter, could be felt. On opening, the viscus was found to contain multiple pigmented calculi. At the fundus there was a firm, cystic thickening of the wall, with normal serosal and mucosal coverings, but no central pit.

Histology.—Sections showed changes in all respects similar to *Case* 1. Body of the gall-bladder normal: fundal nodule consisted of marked, penetrating epithelial sinus formation, with muscular hypertrophy.

Case 4.—Male, aged 46 years. Autopsy case: death from coronary thrombosis.

THE GALL-BLADDER (8 × 3·5 cm.).—Externally the gall-bladder appeared normal, save for an opaque, thickened projection at the fundus. On opening, no stones were found in the lumen. At the fundus there was

a typical umbilicated nodule, 1 cm. in diameter, with normal serosal and mucosal coverings. The rest of the gall-bladder wall appeared normal, but the opening of the cystic duct was very narrow.

Histology.—Sections showed changes in all respects similar to *Cases* 1 and 3.

Case 5.—Female, aged 50 years. Twelve-months' history of attacks of epigastric pain, radiating to the interscapular area: attacks, not related to food, occur at intervals of 1–5 weeks, and usually last about 12 hours. No history of jaundice. No significant clinical signs.

CHOLECYSTOGRAM.—The preliminary film shows some calcified opacities in the right upper quadrant, presumably

FIG. 566.—*Case* 5. Preliminary film, showing two large calculi, presumably in the fundus of the gall-bladder, with a third smaller stone probably in the cystic duct.

gall-stones (*Fig.* 566). From their position it appears that the larger stones are in the fundus, with a smaller one in the cystic duct. In the films taken after its administration there is a good concentration of dye immediately surrounding the larger calculi, but only a thin, irregular streak of dye is seen in the gap between these and the small, separate stone (*Fig.* 567). Little contraction occurs after the fatty meal. In all the films, whether taken prone or erect, all the stones retain the same position relative to one another. The appearances suggest a stricture of the gall-bladder, with stones in the distal loculus and a separate calculus in the cystic duct.

OPERATION (July 13, 1955, L. P. LeQ.).—Cholecystectomy.

THE GALL-BLADDER (9 × 2·5 cm., *Fig.* 568).—The entire gall-bladder was thickened and opaque, and at its mid-point a stricture could be felt. Two calculi could be felt distal to this stricture, and a further smaller one impacted in the cystic duct. On opening the gall-bladder the proximal loculus was found to be full of white, putty-like material; this loculus was lined by apparently normal mucosa and had slightly thickened walls. The distal loculus was finely trabeculated, with thickened walls containing small cysts: this thickening was particularly marked at the site of the stricture, with cystic spaces up to 3 mm. diameter. The opening of the cystic duct was very narrow, with normal duct beyond: the narrowing appeared to be caused by a diaphragm of mucous membrane.

Histology.—Sections from the proximal loculus show a mucosal lining consisting of tall, columnar cells, with occasional superficial epithelial sinuses. The muscularis is of normal thickness, but there is some subserous fibrosis. At the site of the narrowing there is an abrupt

FIG. 567.—*Case* 5. Cholecystogram, showing a good concentration of dye around the larger calculi, but only a thin streak between them and the small calculus. (*See text* for interpretation.)

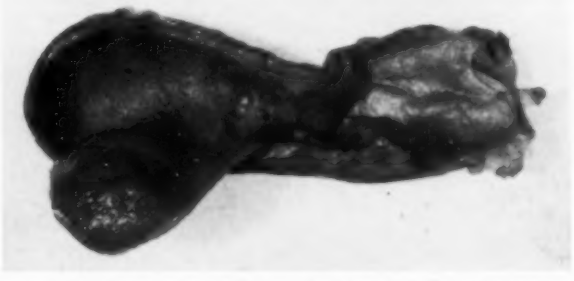


FIG. 568.—*Case* 5. Photograph of the excised gall-bladder. The entire viscus is thickened, and at its midpoint this thickening is especially marked, with formation of a stricture with cystic walls. The proximal loculus was full of white, putty-like material. Two calculi lay in the distal loculus, with a third impacted in the cystic duct.

change, with epithelial sinus formation, giving rise to deep protrusions extending through the hypertrophic muscle coat, and ending in large cyst-like spaces. This is associated with diffuse, chronic inflammatory-cell infiltration and fibrosis of the perimuscular layer. The walls of the distal loculus show similar, but less marked, changes and at the fundus there is an exaggeration of the whole process, with some mucus-cell formation in the deeper sinuses.

Case 6.—Female, aged 48 years. For over ten years has had attacks of epigastric pain, radiating to back, with flatulence and bitter regurgitation: pain especially brought on by fatty foods. Physical examination—slightly tender in epigastrium.

CHOLECYSTOGRAM.—There is a circular, calcified opacity about the size of a small cherry in the right hypochondrium, lying at about the mid-point of the

abdomen from before backwards. There are also one or two small flecks of calcification in the same area. The gall-bladder concentrates the dye well, and contracts down after a fatty meal. The film taken after the fatty meal shows several small linear or spherical shadows lying around the periphery of the fundus. The calcified opacity bears a constant relationship to, but is separated from, the dye-filled gall-bladder (*Figs.* 569, 570).

FIG. 569.—*Case* 6. Cholecystogram. The gall-bladder concentrates the dye well. Distal to, and separated from, the irregular 'fundus' is a calcified opacity previously noted in the preliminary film.

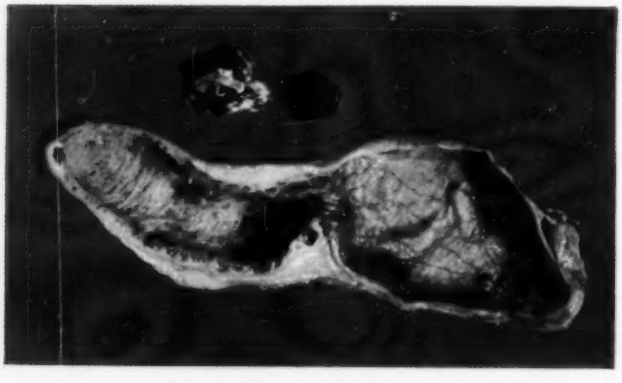


FIG. 571.—*Case* 6. Photograph of the excised gall-bladder. At its mid-point there is a tight stricture. At the site of the stricture and surrounding the distal loculus the walls are thickened, trabeculated, and cystic, whereas the wall of the proximal loculus is normal. The distal loculus contains a single, pigmented calculus surrounded by white, pultaceous material.

OPERATION (July 15, 1953, L. P. LeQ.).—Cholecystectomy.

THE GALL-BLADDER (10 × 3 cm., *Fig.* 571).—Externally the gall-bladder showed a slight constriction at about its mid-point. Between this point and the cystic duct the viscus appeared essentially normal. The distal segment had thickened walls, opaque yellow in colour, and could be felt to contain soft, compressible material surrounding a calculus. On opening there was found to be a tight stricture at the mid-point. Distal to this the greatly thickened, trabeculated wall contained multiple cystic spaces, many of them containing pigmented calculi, and the lumen was filled with white, pultaceous material surrounding a single, mixed calculus. The stricture itself was caused by extreme thickening and inward projection of the wall, with well-marked cysts at this point. The proximal loculus appeared normal.

FIG. 570.—*Case* 6. Cholecystogram. Film exposed after the patient had taken a fatty meal. The gall-bladder has contracted well, and some dye-filled spaces can now be seen around the periphery of the 'fundus'. The separate calcified opacity is also shown.

Histology.—The wall of the proximal loculus was normal on section. The wall of the distal loculus was grossly thickened, with muscular hypertrophy and chronic inflammatory changes in the perimuscular layer. There were numerous epithelial diverticula, penetrating through the muscle coat, with cyst formation, many containing pigmented concretions.

Case 7.—Male, aged 48 years. Twelve-years' history of intermittent epigastric pain, very suggestive of peptic ulcer. No significant physical signs. On one occasion during this time a barium meal had demonstrated a duodenal ulcer, but two other barium meals had shown only deformity of the duodenal cap.

CHOLECYSTOGRAM (Oct., 1955, Royal Northern Hospital).—The gall-bladder concentrates the dye well, and contracts well after a fatty meal. No calculi seen. The gall-bladder is divided into two unequal loculi by a broad, smooth stricture. The smaller, distal loculus is slightly irregular in outline and is surrounded by a halo of irregular, dye-filled spaces (*Fig.* 572). In the film taken after a fatty meal the two loculi appear completely separated, and the extraluminal dye-filled spaces are more marked (*Fig.* 573).

OPERATION (Nov. 27, Mr. B. H. Hand).—Gall-bladder adherent to duodenum: no evidence of duodenal ulcer. Cholecystectomy performed.

THE GALL-BLADDER (9 × 4 cm., *Fig.* 574).—Externally the gall-bladder showed a distinct waist: proximal to this it appeared normal but distally was opaque and thickened. On opening, a stricture was seen: the walls of the distal loculus were 1 cm. thick, containing obvious cystic spaces up to 0·5 cm. diameter. Multiple, pigmented concretions present in the cysts but no calculi in either loculus. Proximal loculus appeared normal.

Histology.—Sections show (1) normal appearances in the wall of the proximal loculus, (2) changes in the wall of the distal loculus in every way similar to *Case* 6: penetrating epithelial sinus formation, muscular hypertrophy, and perimuscular chronic inflammatory changes all well marked.

FIG. 572.—*Case* 7. Cholecystogram. The gall-bladder is divided into two unequal portions by a broad, smooth stricture. The walls of the distal loculus are irregular, and in the original film extraluminal dye-filled spaces could be seen.

FIG. 574.—*Case* 7. Photograph of the excised gall-bladder. A narrow stricture is present at the mid-point of the viscus. Proximal to this the gall-bladder is normal, but the wall of the distal loculus is grossly thickened, with many cystic spaces containing pigmented calculi.

Case 8.—Female, aged 37 years. For fourteen years had suffered from indigestion, particularly after fatty foods. No history of jaundice and no significant physical signs when seen as an out-patient, but when admitted for operation was jaundiced, with pale stools and dark urine.

CHOLECYSTOGRAM.—The gall-bladder concentrates the dye well but is of unusual shape: the proximal portion appears normal, but in place of the body and fundus there is a narrow, irregular dye-filled projection (*Fig.* 575). The appearances suggest that the wall of the distal gall-bladder is grossly thickened, reducing the lumen to a narrow slit.

OPERATION (Aug. 4, 1954, Mr. N. E. Stidolph).—Cholecystectomy and exploration of common bile-duct.

THE GALL-BLADDER (6 × 3 cm.).—The proximal portion of the gall-bladder appeared normal, but throughout the distal portion the walls were opaque, thickened, and œdematous, greatly reducing the calibre of the lumen. Calculi were present in the proximal portion of the viscus.

Histology (Sections kindly supplied by Dr. S. Robinson, Whittington Hospital).—Section of the distal portion of the gall-bladder shows gross thickening of the wall, with epithelial sinus formation and numerous, dilated, extramuscular protrusions. The epithelium lining the sinuses shows mucus-cell formation. There is hypertrophy of the muscularis, with advanced chronic inflammatory changes in the perimuscular layer. Pigmented concretions are present in many of the extramuscular cysts. The wall of the proximal portion shows thickening from chronic inflammatory changes, but little muscular hypertrophy and penetrating sinus formation.

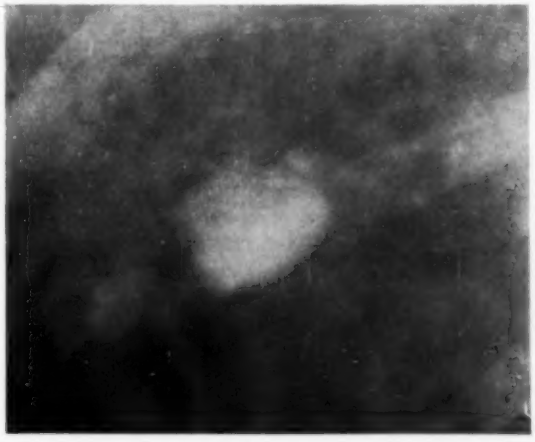


FIG. 573.—*Case* 7. Cholecystogram. Film exposed after the patient had taken a fatty meal. The gall-bladder has contracted well. The stricture now appears complete, with separation of the two loculi.

FIG. 575.—*Case* 8. Cholecystogram. The gall-bladder concentrates the dye well, but is of bizarre shape. The proximal portion appears normal, but in place of the body and fundus there is an irregular, dye-filled projection.

Case 9.—Female, aged 36 years. Twelve-months' history of attacks of epigastric pain, not related to meals but associated with flatulence. No history of jaundice. Slight tenderness in right hypochondrium, otherwise no abnormal clinical signs.

CHOLECYSTOGRAM.—The gall-bladder concentrates the dye well, contains no calculi, and contracts well. The gall-bladder shadow is surrounded by multiple, smaller shadows, most marked in the region of the neck and

fundus: in these areas the shadows are spherical or flask-shaped, but opposite the body of the gall-bladder they are smaller and linear, lying parallel to the gall-bladder (*Fig.* 576). These extravesical shadows, most clearly seen in the film taken after a fatty meal, are presumably dye-filled diverticula.

OPERATION (Oct. 6, 1954, Mr. P. T. Savage).—Cholecystectomy and exploration of the common bile-duct.

FIG. 576.—*Case* 9. Cholecystogram. Film exposed after the patient had taken a fatty meal. The gall-bladder concentrates the dye well and has contracted well. The main shadow is surrounded by multiple, smaller shadows most marked at the neck and fundus. In these areas the extraluminal shadows are flask-shaped, but opposite the body of the gall-bladder they are linear.

THE GALL-BLADDER (11 × 2·5 cm.).—The gall-bladder was thick-walled, opaque, and felt to contain many small stones. Before opening, the gall-bladder was filled with 50 per cent diodone and an X-ray picture was taken, the film clearly showing multiple diverticula communicating with the lumen, these diverticula being particularly marked at the fundus and near the proximal end of the gall-bladder (*Fig.* 577). On opening, the gall-bladder was seen to be divided into two unequal loculi by a stricture 2 cm. in length. The smaller, proximal loculus appeared normal. At the site of the stricture the gall-bladder wall was grossly thickened, with cystic areas up to 0·5 cm. diameter, containing pigmented calculi. The walls of the distal loculus were trabeculated and thickened, showing changes similar to the strictured area. There was, in addition, an umbilicated fundal nodule, similar to that in *Cases* 1–4 (*Fig.* 578). There were no calculi in the lumen of either loculus.

Histology.—Sections show the small, proximal loculus to be composed of essentially normal gall-bladder wall. At the site of the stricture there are gross epithelial diverticula, with large cyst-like spaces outside the hypertrophied muscularis, some of them containing pigmented concretions. This process extends to a lesser extent throughout the remainder of the wall and is again marked at the fundus.

Case 10.—Female, aged 44 years. During the last three years has had six attacks of severe, epigastric pain, not apparently related to meals. No history of jaundice. Some upper abdominal tenderness, but no other significant clinical signs.

CHOLECYSTOGRAM.—The preliminary film shows a collection of small opacities in the right upper quadrant of the abdomen, presumably gall-stones. After dye, the gall-bladder concentrates, fills, and contracts well, and the opacities are seen to be superimposed on the gall-bladder shadow. In all the films exposed after taking dye there is a cluster of irregular opacities, presumably dye-filled spaces (*Fig.* 579), lying in a semicircular area adjacent to, but just beyond, the fundus. These

FIG. 577.—*Case* 9. Radiograph of the excised gall-bladder, after it had been filled with 50 per cent diodone. Multiple diverticula communicating with the lumen of the gall-bladder can clearly be seen: the largest lie in the regions of the neck and fundus.

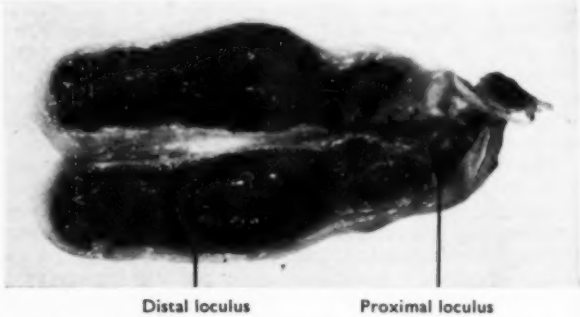


FIG. 578.—*Case* 9. Photograph of the excised gall-bladder. The gall-bladder is divided into two unequal loculi by a broad, cystic stricture. The small, proximal loculus is normal. The walls of the distal loculus are thickened with a cystic umbilicated nodule at the fundus. Multiple, small, pigmented intramural calculi can be seen.

opacities are least well seen in the film taken after a fatty meal.

OPERATION (April 23, 1954, Mr. J. Carron Brown).—Cholecystectomy and exploration of common bile-duct: patient has been well since operation.

THE GALL-BLADDER (9 × 2·5 cm.).—Externally the gall-bladder was whitish in colour, with a firm protuberance at the fundus. On opening the specimen this protuberance was found to consist of a cystic tumour

FIG. 579.—*Case* 10. Cholecystogram. The gall-bladder concentrates the dye well. Distal to the fundus is an irregular collection of dye-filled spaces.

1·0 cm. across, with a well-marked but eccentrically placed dimple on its mucosal surface. This dimple and the cystic spaces are clearly shown on radiography of the excised gall-bladder after distension with diodone (*Fig.* 580). The mucosa and serosa covering this fundal tumour appeared normal: the cystic spaces contained many small pigmented calculi. The remainder of the gall-bladder contained many similar but larger calculi, but otherwise appeared normal, except for a diaphragm-like stricture 1 cm. from the opening of the cystic duct, composed of cystic thickening of the gall-bladder wall.

Histology.—Sections show the body of the gall-bladder to be essentially normal. The stricture consists of muscular hypertrophy, with penetrating epithelial sinus formation and some fibrosis. The lesion at the fundus is in all respects similar to those in *Cases* 1–4 with mucus-cell degeneration in the sinuses (*Fig.* 581).

Case 11.—Male, aged 55 years. Autopsy specimen: death from carcinoma of bronchus: no history of symptoms referable to biliary system.

THE GALL-BLADDER (12 × 4·5 cm.).—Externally the gall-bladder showed a well-marked bulge at the fundus, and a slight constriction 2 cm. from the cystic duct: at both these sites the wall was opaque and thickened. On opening the viscus a typical cystic tumour, 2 cm. across, was seen at the fundus, with a central pit and all the other features seen in *Cases* 1–4. 2·5 cm. proximal to the opening of the cystic duct there was cystic thickening of the gall-bladder wall, forming a slight stricture. The wall between these two lesions appeared normal. No calculi in the gall-bladder.

Histology.—The appearances were in all respects similar to those in *Case* 10.

Case 12.—Female, aged 23 years. Two-months' history of mild indigestion, with pain in the right hypochondrium, particularly after fatty foods. On two occasions she had had two attacks of severe pain, suggestive of biliary colic. Slight tenderness in right hypochondrium was the only significant physical sign.

FIG. 580.—*Case* 10. Radiograph of the excised gall-bladder, after it had been filled with 50 per cent diodone. The soft-tissue shadow of the fundal nodule is clearly seen, with dye filling the eccentric pit and several intramural diverticula.

FIG. 581.—*Case* 10. Photomicrograph of the fundal nodule. Cystic spaces can be clearly seen lying outside the muscle coat. Many of these spaces contain calculous debris. The adjacent gall-bladder wall at either edge is normal. (× 3.)

CHOLECYSTOGRAM.—The gall-bladder concentrated the dye well and contracted well after a fatty meal. No evidence of calculi. In several of the films there was a small marginal filling-defect near the fundus, suggestive of a papilloma.

OPERATION (Nov., 1955, Mr. H. E. Lockhart-Mummery).—Cholecystectomy.

THE GALL-BLADDER (9 × 3 cm., *Fig.* 582).—Externally the viscus appeared normal, save for a bulge at the fundus; this bulge was normal to touch, with a thickened rim at its base. On opening, a circumferential thickening of the wall was seen, forming a slight stricture 1 cm. from the fundus. Apart from this no abnormality was apparent.

Histology.—The entire proximal gall-bladder appeared normal. At the site of the stricture there was muscular hypertrophy with some penetrating epithelial sinus formation, and similar but less marked changes were present throughout the fundus distal to the stricture.

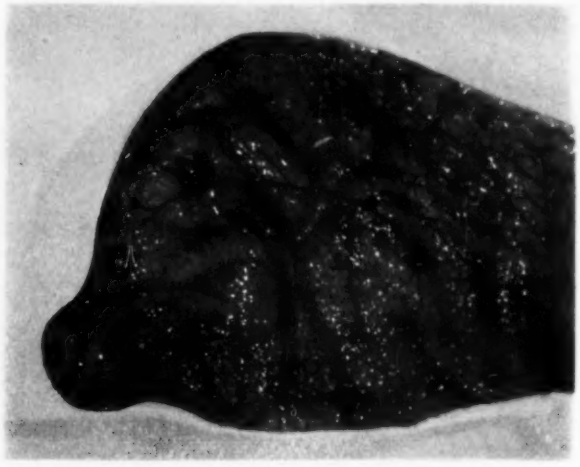


FIG. 582.—*Case* 12. Photograph of the excised gall-bladder, which was in all respects normal except for a slight but distinct stricture just proximal to the fundus.

DISCUSSION

MORBID ANATOMY

The outstanding lesion in cholecystitis glandularis proliferans is the formation of epithelial sinuses (Rokitansky-Aschoff sinuses), which penetrate through the muscularis of the gall-bladder, to expand in the perimuscular (subserous) layer, with the formation of cyst-like spaces. Associated with this there is invariably localized hypertrophy of the muscle coat, and often chronic inflammatory changes and intramural calculus formation. On macroscopical section the formation of cystic spaces external to the muscularis is obvious, but microscopy shows that in fact sinus formation takes place internally as well. On the mucosal side such sinus formation gives rise to polypoid projections, usually only microscopic in size, and the main thickening of the gall-bladder wall is undoubtedly due to the penetration of epithelial sinuses outwards, through the interstices of the muscle wall. Once in the perimuscular layer the sinuses tend to dilate, with the formation of cyst-like spaces.

Initially at any rate all the sinuses external to the muscularis are connected with the lumen of the gall-bladder, but it seems probable that in many the narrow necks become obliterated where they pass through the muscularis, leading to the formation of true cysts. However, whether complete obstruction occurs or whether the lumen at the neck remains patent, it is clear that there will be stagnation in the distal, dilated portions of the sinuses. This, no doubt, accounts for the intracystic calculus formation so frequently seen. In all the 5 cases reported here in which the lumen of the gall-bladder also contained stones, these calculi were similar in appearance to those in the cysts, suggesting that they originated in such crypts, passed into the lumen of the gall-bladder whilst still minute, and then enlarged there.

In the deeper portions of the crypts the normal, tall columnar cells of the mucosa were frequently seen to have been replaced by mucus cells, well shown by staining with muci-carmine. This change is probably a degeneration as a result of irritation from the inspissated contents of the crypts. King and MacCallum (1931) also report that the mucosa deep in the sinuses may show cells of a gastric type, but we have not observed this. The other two characteristic microscopical changes seen in the condition are chronic inflammatory infiltration around the sinuses and, most striking, thickening and hypertrophy of the muscle coat, strictly limited to the confines of the lesion itself. The exact significance of this muscular hypertrophy is far from clear, and is discussed below. In all the cases reported here it was most noticeable that the lesions were distinctly circumscribed and that the remainder of the gall-bladder, in some cases the greater part of it, was normal.

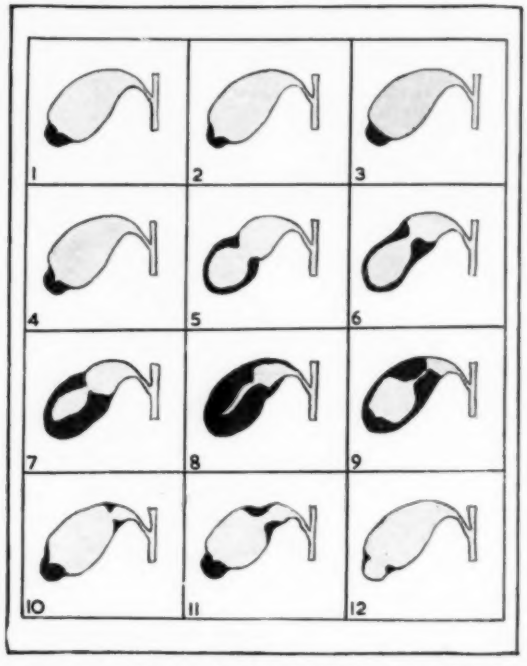


FIG. 583.—Diagram showing the distribution of the lesions in the cases reported; the lesion is represented by thickening of the wall of the gall-bladder. The predominance of fundal nodules and strictures is clearly shown.

The gross macroscopical changes which the condition may cause vary greatly, as illustrated by the cases reported. None of the present series showed distinct polypi projecting into the lumen of the gall-bladder, as described by King and MacCallum (1931), though microscopic polyps were seen in several. The anatomical type of change in our cases is shown diagrammatically in *Fig.* 583, which brings out clearly the remarkable tendency for the condition to produce either fundal nodules or ring strictures.

Indeed it is tempting to believe that the changes seen in *Cases* 5–9 are in fact developments from these two basic lesions, as a result of (*a*) extension of a fundal nodule, with expansion of its central pit, or (*b*) the distal extension of a stricture, or (*c*) the simultaneous development of a fundal nodule and stricture, as in *Case* 11, which later spread and coalesce. There is no evidence to support such a hypothesis, apart from its attractiveness, but the predominance of the two types of lesion is most striking, though its significance is far from clear.

SPECIFICITY OF THE LESION

In view of the facts that (*a*) epithelial sinuses, even penetrating through the muscle coat, are seen in the normal gall-bladder and are commonly found in cases of chronic cholecystitis, and (*b*) that cholecystitis glandularis proliferans appears to consist of an excessive formation of such sinuses, it might be argued that it is unjustifiable to burden with so cumbersome a title what appears to be simply a variant of a common condition. However, whereas chronic cholecystitis almost invariably affects the entire gall-bladder, it was most noticeable that in all save one of our cases the lesions were strictly circumscribed and the remainder of the gall-bladder was unaffected. Further, whereas chronic cholecystitis is usually associated with stones, this association is by no means the rule in cholecystitis glandularis proliferans, and in less than half our cases (5 out of 12) were there calculi in the lumen of the gall-bladder. In addition, in the cases we have observed the epithelial sinus formation and muscular hypertrophy have been the predominant microscopical lesion, not the chronic inflammatory changes. For these reasons, we submit that, in the present state of our knowledge, it is justifiable to segregate this type of case under a special title.

It is remarkable that hitherto the fact that often in this disease the greater part of the gall-bladder is normal has escaped comment. In some of the early descriptions, in which the lesions, especially fundal nodules, were considered to be benign neoplasms, it is implied that the rest of the viscus was normal (Wellbrook, 1934). Within recent years several cases with stricture formation, detected on cholecystography, have been reported, but in the majority of these no mention is made of the macroscopical or microscopical appearances of the proximal loculus, though March (1948) reports that to the naked eye the proximal loculus in his case appeared normal.

This concept of the normality of the unaffected portion of the viscus is not accepted by King and MacCallum (1931), who defined the condition of cholecystitis glandularis proliferans as "a circumscribed or diffuse thickening of the wall of a chronically inflamed gall-bladder, characterized by excessive proliferation of, and invasion of, the wall by epithelium, forming crypts, with dilatation, of some of these crypts to form cysts". This definition implies that the entire gall-bladder is the site of chronic inflammatory changes, and later in their paper they state specifically: "In the cases examined there has been evidence of chronic cholecystitis in the wall away from, as well as in, the specially thickened tissue." From the description of their 25 cases it appears that in most the condition was fairly generalized, and 21 had stones in the gall-bladder. In a later paper King (1953) describes 2 further cases which were diagnosed on cholecystography. In one of these there was a typical stricture and the wall of the proximal loculus undoubtedly showed chronic inflammation, but it contained far fewer sinuses than the wall of the distal loculus: in the second case the gall-bladder was generally thickened, but the intramural cysts were prominent only near the fundus.

At first sight it seems almost impossible to correlate the findings of King and MacCallum (1931) and King (1953) with those in the cases described here. We would suggest that the explanation lies in the relationship between the epithelial sinus formation and the chronic inflammatory changes, and that two distinct conditions may affect the gall-bladder:—

1. Ordinary chronic cholecystitis: a diffuse condition, affecting the entire gall-bladder, in the course of which penetrating epithelial sinuses may form, but usually not to a marked degree.

2. Cholecystitis glandularis proliferans, in which the essential lesion is the localized development, at one or more sites, of penetrating epithelial sinuses and muscular hypertrophy, with chronic inflammatory changes of varying degree developing around these sinuses and their cystic terminations. Later, as the result usually of calculus formation in the lumen of the gall-bladder, the entire gall-bladder may become the site of ordinary chronic cholecystitis, resulting in thickening of the previously unaffected portions of the viscus.

It will be seen that in advanced cases it may be difficult to differentiate the two conditions, especially if the sinus formation is at all marked in (1), and in (2) has become over-run and strangled by excessive fibrosis. King and MacCallum (1931) indeed remark that they have seen several specimens which on first examination appeared to have cholecystitis glandularis proliferans but on further inspection turned out to have chronic cholecystitis. It is to be noted that their cases were described over twenty years ago, when radiology and surgery were not as advanced as to-day and when cholecystectomy was not performed for such mild symptoms as nowadays. In contrast, the cases described here were drawn from a community provided with abundant specialist services and most had comparatively mild symptoms which would probably not have led to cholecystectomy twenty-five years ago. As a result, King and MacCallum were likely to have observed specimens showing late changes, whereas our cases were more likely to be in their early stages.

We would suggest, therefore, that the term 'cholecystitis glandularis proliferans' be reserved for cases in which (*a*) the lesion is circumscribed, or apparently was so at one stage, and (*b*) the essential features of the lesion are the excessive production of penetrating epithelial sinuses, with localized muscular hypertrophy. It is notoriously confusing and undesirable to change the significance of terms previously coined by other workers, but we feel that in this instance such a course is preferable to burdening the literature with yet another name, though should further studies support the hypothesis outlined it might then be desirable to give the condition another title.

AETIOLOGY

In the past the condition has often been described as a benign neoplasm of the gall-bladder. Thus, in 1933 Phillips described 500 examples of ' papilloma ' of the gall-bladder, many of them only microscopic in size. However, from his description it seems clear that at least the great majority of these ' papillomata ' were either cholesterol polyps, or polypi of the type illustrated in *Fig.* 564. In 1934 Wellbrook similarly described 67 adenomata of the gall-bladder : all but

FIG. 584.—Gall-bladder contraction as seen under the fluoroscope after the ingestion of motor (fat) meal. 1, Gall-bladder at rest ; 2, 3, Usual types of contraction ; 4, Unequal contraction of longitudinal bundles ; 5, Vigorous contraction, frequently seen in gall-bladders containing stones. (*After Levene*, 1932.)

two of these were at the fundus, most of them were umbilicated, and microscopically they were identical with the lesions in *Cases* 1–4. Writing in 1942, Shephard, Walters, and Dockerty state : " The benign neoplasms of the gall-bladder are polypus, adenomyoma, and fibroma." Under the title of adenomyoma they give a clear description of dimpled, cystic, fundal nodules such as those seen in *Cases* 1–4, and agree that the condition is the same as that described by King and MacCallum (1931) as cholecystitis glandularis proliferans, but they maintain it is neoplastic in nature.

The distinction between hyperplasia and true neoplasia is a notoriously difficult one, and in view of the fact that in the condition described there is an undoubted localized excess of epithelial tissue it is possible that it might be truly neoplastic in nature. However, nowadays it is generally considered that the condition is not neoplastic. Both King and MacCallum (1931) and King (1953) specifically state their opinion that the condition is neither neoplastic nor precancerous. Kerr and Lendrum (1936), in their report of one of the very few genuine examples of papilloma of the gall-bladder, state : " Much confusion has arisen within the last twenty years through the application of the term ' papilloma ' to lesions which many are unable to accept as in any true sense neoplastic." They go on to discuss polypi of the type illustrated in *Fig.* 564 : " Nothing is gained by attributing to this lesion a name which implies that it is essentially neoplastic and it would seem preferable to use the term ' cholecystitis polyposa ' or, as suggested by King and MacCallum, ' cholecystitis glandularis proliferans '."

Unequivocal benign neoplasms of the gall-bladder are remarkably rare. We have been unable to find any record of an undoubted adenoma. Kerr and Lendrum (1936) were able to find reports of only 7 cases they could accept as true papillomata, though since then a few more cases have been described (notably Brown and Cappell, 1937 ; Griffiths, 1956 ; Morrison and Stewart, 1956). In all these cases the appearances, both macroscopic and microscopic, were entirely different from those in the cases described here. In cholecystitis glandularis proliferans the mucosa is regular and uniform, with an epithelial layer one cell in thickness with none of the stigmata of hyperactivity. There can be no doubt that the epithelial diverticula represent mere overdevelopment of perfectly normal structures, the Rokitansky-Aschoff sinuses. Further, the epithelial changes are constantly associated with remarkable changes in the neighbouring tissue, namely muscular hypertrophy, and are commonly localized in one of the two peculiar forms already stressed. None of these facts is consistent with the lesion being neoplastic, and the conclusions of Kerr and Lendrum (1936) seem inescapable.

In considering the aetiology an explanation must be found for (1) the constant association of muscular hypertrophy localized to the area of epithelial change ; (2) the normality of the remainder of the gall-bladder, at least in the early stages of the disease ; (3) the tendency of the lesions to take the form of either (*a*) fundal nodules, or (*b*) strictures. It seems clear that an increase of pressure within the gall-bladder cannot account for such strictly localized diverticula formation, a conclusion reached on other grounds by King (1953). Further, it is by no means clear whether the muscular or epithelial changes are the primary event, or whether the two develop together. However, the constant association of the two, reminiscent of diverticulosis of the colon, strongly suggests an essentially mechanical aetiology, and it may well be that the condition arises as the result of some disturbance in the normal contraction and motility of the gall-bladder.

Surprisingly little appears to be known about the manner in which the human gall-bladder contracts to evacuate its contents, but such information as is available is of great interest in relation to this matter. Boyden (1928) made radiographic studies of the gall-bladder emptying in 24 apparently normal students. He found that within two minutes of giving fat the gall-bladder begins to contract, and Boyden describes the contractions as follows : " In each instance the fundus of the organ becomes narrower and in several cases the relative proportions of the body and fundus are reversed—as if the bile were being compressed from below, causing the body and neck of the organ to bulge." Levene (1932) also describes the contraction of the gall-bladder as seen radiographically. He writes : " Gall-bladder contractions of divers varieties are encountered, the type most frequently seen consisting of slight localized alterations of contour along the borders of the vesicle, most marked at the fundus. These contractions appear to be cyclic and are accompanied by a tonic contraction of all the muscle-fibres, which progressively increase until the vesicle has attained its smallest possible size." Levene illustrates his article with the tracings reproduced in *Fig.* 584, and it can be seen that the portion of the gall-bladder contracting is remarkably similar to that involved in many of our cases (*Fig.* 583).

Apart from the localized muscular hypertrophy, there is no evidence that patients with this condition have, in fact, any abnormality in contraction of their gall-bladders. Further, it is not clear why such a disturbance should lead to diverticulum formation,

though once the sinuses have developed it is easy to imagine their necks being obstructed by the hypertrophic muscle-bundles. In the present state of our knowledge it does not seem possible to reach firm conclusions upon the aetiology of this condition, but in view of the considerations set out above, we would tentatively suggest that (*a*) cholecystitis glandularis proliferans arises as a disturbance of contraction of the gall-bladder, (*b*) the essential lesions are the muscular hypertrophy and epithelial sinus formation, and (*c*) the inflammatory changes and intramural calculus formation are secondary to stagnation in these sinuses.

CLINICAL ASPECTS

Clinically the condition gives rise to no symptoms by which it may be distinguished from ordinary cholecystitis with gall-stones. Indeed in many cases, exemplified by those found at autopsy, it probably gives rise to no symptoms at all. In the majority of cases the diagnosis is only made after the gall-bladder has been removed, but with the improved techniques used in modern radiology it is often possible to recognize the condition on cholecystography. In recent years several cases have been recorded in which Rokitansky-Aschoff sinuses were demonstrated in this way. Describing such a case, Sutton (1955) states that up to that time only 11 such cases had been described, and that the first was reported by March (1948). Since then a further case, making 13 in all, has been reported by Kamdar (1955), but it is certain that many examples have gone unrecorded. However, on the assumption that the distinction between cholecystitis glandularis proliferans and chronic cholecystitis with marked sinus formation is valid, it is by no means certain that all these 13 cases had the former condition. From the evidence provided it seems probable, though not certain, that the lesions were localized and very similar to those described here, in the cases reported by March (1948), Bean and Culver (1950), King (1953, one of the two cases), Sukman and Daron (1953), and Ross, Finey, and Evans (1955). In the remaining cases (Ackermann, 1948; Åkerlund and Rudhe, 1950; Glücker, 1951; Lawler, 1952; Zinober, 1952; King, 1953, one case; Lapointe, 1953; Stalker, Davies, and Guest, 1955; Sutton, 1955; Kamdar, 1955) it would appear that there was a generalized thickening of the gall-bladder wall, though in some of these reports there is no description of the specimen itself and it is possible that a small, normal proximal loculus was overlooked.

Whilst it is true that March (1948) was the first to report the demonstration of Rokitansky-Aschoff sinuses on cholecystography, this was not, however, the first occasion on which cholecystitis glandularis proliferans had been demonstrated radiographically. In 1930 Kirklin reported a case which on cholecystography showed a gall-bladder with good concentration, but with a "small, round, transradiant area near the fundus. A diagnosis of a normally functioning gall-bladder with a single stone was returned. At operation an adenomyoma was found, but no stone." From the description it seems certain that the lesion was not, as thought by Kirklin, a neoplasm, but a fundal nodule of the type illustrated in *Cases* 1–4, and this case constitutes, as far as we can ascertain, the first recorded example of the demonstration of cholecystitis glandularis proliferans by radiography. This case is referred to again by Kirklin in 1931, in which year Hefke (1931) also reported a case showing a filling-defect on cholecystography which turned out to be an 'inflammatory lesion', probably a type of this condition. Again, in 1935 Moore reports 2 cases, one of which was clearly a fundal nodule similar to *Cases* 1–4. McWhirter (1935) discusses at some length the diagnosis of 'adenoma' on cholecystography: again it seems certain from his description, from the films of two cases, and from the illustration of one specimen, that the lesions were similar to those in *Cases* 1–4, and this paper appears to be the first mention of the subject in British literature. In respect of strictures, Vastine (1934) reported a case very similar to *Case* 6, with an undoubted ring of Rokitansky-Aschoff sinuses at the site of the stricture, though it appears that the 'distal loculus' may have consisted of a single, large epithelial diverticulum. Paillard and Paillard (1936) also reported 4 cases in which the gall-bladder was said to be bilobed: in 2 of these the radiographs clearly resemble those of case 7, but unfortunately neither of these cases was treated by surgery, but by 'la cure de Vittel'.

The radiographic appearances in any given case depend entirely upon the macroscopic changes in the gall-bladder wall and the extent to which, in late cases, the concentrating power of the gall-bladder is impaired, but the three characteristic signs are (*a*) a fundal filling-defect, sometimes showing a central pit, (*b*) a stricture, or (*c*) dye-filled spaces around the periphery of a greater or lesser part of the gall-bladder shadow. This last sign may be present by itself, or sometimes in association with one of the other two. There may or may not be gall-stones demonstrable as well. All of these various appearances are illustrated by the cases reported here. It is noteworthy that in nearly all the relevant case reports the authors comment that the dye-filled sinuses show up most clearly in the films taken after ingestion of a fatty meal, and we also found this to be true in some of our cases (*Cases* 6–8, 10).

With regard to treatment, it is clear that if the patient's symptoms suggest gall-bladder disease and the cholecystogram shows changes of the type described, then cholecystectomy is indicated. The results in these cases appear to be as good as in those in which the operation is performed for cholelithiasis.

SUMMARY

1. Twelve cases of cholecystitis glandularis proliferans are reported. In each case the condition gave rise to a macroscopic, localized lesion in the gall-bladder, the remainder of the viscus being normal.

2. In 4 of the cases the lesion was found incidentally at autopsy. The remaining 8 cases were encountered in clinical practice, and in these cases the lesions were apparent on cholecystography.

3. It is suggested that cholecystitis glandularis proliferans is not just a variant of ordinary chronic cholecystitis, but that (*a*) it in fact constitutes a specific disease entity, and (*b*) that the essential

feature of the condition is a localized area of penetrating epithelial sinus formation with muscular hypertrophy.

4. In view of the nature and distribution of the lesions, it is suggested that the condition results from some disturbance in the normal contraction of the gall-bladder.

5. The clinical and radiological features of the condition are described.

Acknowledgements.—We are indebted to Mr. N. E. Stidolph, Mr. P. T. Savage, and Mr. H. E. Lockhart-Mummery for providing us with the details of their patients and enabling us to examine the specimens, and for allowing us to report their cases; to Dr. L. S. Carstairs and Dr. G. Osborne for permission to reproduce radiographs taken in their Departments; and to Dr. A. C. Thackray for his assistance with the photomicrographs.

REFERENCES

ACKERMAN, A. J. (1948), *Amer. J. Roentgenol.*, **60**, 256.
ÅKERLUND, A., and RUDHE, U. (1950), *Acta radiol., Stockh.*, **33**, 147.
*ASCHOFF, L. (1905), *Verh. dtsch. path. Ges.*, **9**, 41.
BEAN, B. C., and CULVER, G. J. (1950), *Amer. J. Roentgenol.*, **63**, 665.
BOYDEN, E. A. (1928), *Anat. Rec.*, **40**, 147.
BROWN, F. R., and CAPPELL, D. F. (1937), *Brit. J. Surg.*, **24**, 703.
GLÜCKER, L. (1951), *Acta radiol., Stockh.*, **35**, 133.
GRIFFITHS, E. (1956), *Brit. J. Surg.*, **43**, 435.
HALPERT, B. (1927), *Bull. Johns Hopk. Hosp.*, **41**, 77.
HEFKE, H. W. (1931), *Röntgenpraxis*, **3**, 871.
KAMDAR, K. N. (1955), *Brit. J. Radiol.*, **28**, 45.
KERR, A. B., and LENDRUM, A. C. (1936), *Brit. J. Surg.*, **23**, 615.
KING, E. S. J. (1953), *Brit. J. Surg.*, **41**, 156.
— — and MACCALLUM, P. (1931), *Ibid.*, **19**, 310.
KIRKLIN, B. R. (1930), *Proc. Mayo Clin.*, **5**, 336.
— — (1931), *Amer. J. Roentgenol.*, **25**, 46.
LAPOINTE, H. (1953), *J. Canad. Ass. Radiol.*, **4**, 45.
LAWLER, N. A. (1952), *J. Fac. Radiol., Lond.*, **3**, 275.
LEVENE, G. (1932), *New Engl. med. J.*, **207**, 443.
*LUSCHKA, H. (1858), *Z. rationelle Med.*, 3 R., **4**, 189.
— — (1863), *Die Anatomie des menschlichen Bauches.* Tübingen: H. Lauppschen Buchhandlung.
MCWHIRTER, R. (1935), *Brit. J. Surg.*, **23**, 155.
MARCH, H. C. (1948), *Amer. J. Roentgenol.*, **59**, 197.
MOORE, C. (1935), *Amer. J. Roentgenol.*, **33**, 630.
MORRISON, R. J. G., and STEWART, P. D. (1956), *Brit. med. J.*, **1**, 966.
PAILLARD, H., and PAILLARD, M. H. (1936), *J. Radiol. Electrol.*, **20**, 674.
PHILLIPS, J. R. (1933), *Amer. J. Surg.*, **21**, 38.
ROBERTSON, H. E., and FERGUSON, W. J. (1945), *Arch. Path. (Lab. Med.)*, **40**, 312.
*ROKITANSKY, C. (1842), *Handbuch der speciellen pathologischen Anatomie*, **2**, 347. Vienna: Braumüller and Seidel.
ROSS, W. D., FINEY, N., and EVANS, J. A. (1955), *Radiology*, **64**, 366.
SHEPHARD, D. V., WALTERS, W., and DOCKERTY, M. B. (1942), *Arch. Surg., Chicago*, **45**, 1.
*SHIKINAMI, J. (1908), *Anat. Hefte*, **36**, 551.
STALKER, L. K., DAVIES, B., and GUEST, T. P. (1955), *Arch. Surg., Chicago*, **71**, 124.
SUKMAN, R., and DARON, P. B. (1953), *Radiology*, **60**, 714.
SUTTON, D. (1955), *Brit. J. Radiol.*, **28**, 264.
VASTINE, J. H. (1934), *Amer. J. Roentgenol.*, **31**, 603.
WELLBROOK, W. L. A. (1934), *Amer. J. Surg.*, **23**(V.S.), 358.
ZINOBER, M. (1952), *S. Afr. med. J.*, **26**, 35.

* Quoted from HALPERT (1927) and KING (1953).

MESENTERIC VASCULAR OCCLUSION

BY FRANK FORTY
EDGWARE GENERAL HOSPITAL

ACUTE mesenteric vascular occlusion usually presents as an abdominal catastrophe, with no distinguishing features to permit of a precise pre-operative diagnosis. It is estimated to account for about 0·1 per cent of all surgical admissions (Maingot, 1955).

The occlusion may affect the superior or inferior mesenteric vessels, and may be either arterial or venous.

The cause of arterial occlusions is either thrombosis due to atherosclerosis or embolism. That of acute venous thrombosis is usually obscure. It may affect healthy individuals without any warning, and with no apparent cause (Moore, 1941). Occasionally it follows septic conditions such as appendicitis or infected hæmorrhoids, and it may result from portal obstruction in cases of cirrhosis of the liver.

Usually the bowel is gangrenous at the time of laparotomy and resection is the only possible treatment. The overall mortality is extremely high. Of some 700 cases in the literature, only 8·0 per cent of those subjected to resection survived. The prognosis is considerably better in venous than in arterial occlusion. Brown (1940), in a paper devoted to venous mesenteric thrombosis, reviewed 104 collected cases. The mortality among these was 68·2 per cent. A significant factor in the prognosis was the length of bowel involved, the average for the patients who lived being 38·1 in. and for those who died 102·4 in. From 3 in. to 6 in. of healthy bowel should be resected at each end to prevent post-operative extension of the thrombosis to the site of the anastomosis. Anticoagulants have been administered post-operatively as an additional safeguard, as in one of the cases reported by Bintcliffe (1947). In general the prospects of survival are better in the cases of primary venous thrombosis than in those that are secondary to sepsis or portal obstruction. It is possible for venous mesenteric thrombosis of limited extent to recover spontaneously, and some cases of unexplained intestinal hæmorrhage with transient abdominal pain may well be due to this cause.

The records of Edgware General Hospital for the twenty-two years from 1934 to 1955 contain 32 cases of mesenteric vascular occlusion; 17 of the patients were men and 15 were women. The age distribution is given in *Table I*.

Table I.—AGE INCIDENCE

Age	20-30	30-40	40-50	50-60	60-70	70-80	80-90
No. of cases	1	3	1	4	8	11	4

In 17 cases there was definite pathological evidence that the occlusion was arterial and in 7 cases that it was venous.

Of the arterial cases, 16 were due to thrombosis resulting from arteriosclerosis. One case was due to embolus in a woman with mitral stenosis.

Among the cases of venous thrombosis, 1 occurred in a man aged 31 who had cirrhosis of the liver secondary to splenic anæmia for which a splenectomy had previously been performed. A woman, aged 22, the youngest patient in the series, developed venous mesenteric thrombosis during labour at the end of a normal first pregnancy.

The remaining 5 venous thromboses occurred without warning in healthy adults and post-mortem examination revealed no cause.

The average age of the patients with arterial occlusion was 69 years and of those with venous thrombosis 46 years.

The 8 cases in which it is not possible to say whether the occlusion was arterial or venous had an average age of 70 years, a fact which suggests that they were probably arterial thromboses.

Site.—In every case thrombosis, whether arterial or venous, affected the superior mesenteric vessels. The colon was affected together with the small intestine on 6 occasions. In 2 further cases of colonic infarction the small intestine was not involved. In the solitary case of embolism, emboli were found in the superior and inferior mesenteric arteries. These had lodged at a few hours' interval as indicated by two distinct attacks of abdominal pain, during the first of which a small blood-stained stool was passed. This probably corresponded to the inferior mesenteric embolus.

In one case there was infarction of the whole of the small and large intestines as far as the pelvic colon. The inferior mesenteric artery was found to be absent and the whole of the intestine was supplied from the superior mesenteric artery, one large branch of which went to the distal half of the transverse : and to the descending colon.

Symptomatology.—Of the 32 cases, 29 presented as abdominal emergencies and 3 as cases of acute collapse without significant abdominal symptoms in patients aged 76, 77, and 22 years. In the larger group presenting with abdominal symptoms the length of the history varied from 6 hours to 10 days and in one instance it was 8 weeks.

The clinical picture was remarkably uniform. Its essential features were pain, vomiting, and constipation.

Pain was characteristically generalized and constant. Tenderness corresponded with the site of the pain. Some muscle guarding or rigidity was noted in most of the cases. Bowel-sounds were usually audible. No mass was distinctly palpable in any of the cases. Free fluid was demonstrated in several instances. Blood was passed per rectum in 2 cases.

TREATMENT

In 19 cases (59·4 per cent) no operation was performed either because they did not present abdominal symptoms or because they were judged unfit. Many of these patients were moribund on admission and all in this group died.

In 7 cases (21·9 per cent) surgical intervention was limited to a simple exploratory laparotomy. There was one survival in this group. This was a woman aged 70 years who was operated on in 1934 by Dr. Arkley Steel. The presence of mesenteric thrombosis with hæmorrhage into the mesentery was noted and the abdomen was closed. Post-operative recovery was uneventful. The patient was re-admitted to the hospital two years later with abdominal symptoms thought to be due to a further mesenteric thrombosis. No operation was performed on this occasion and the patient again recovered.

In 6 cases (18·7 per cent) a resection was performed. There were 2 survivals in this group.

CASE REPORTS

Case 1 (Mr. D. B. Craig's case).—L. C., female, aged 70 years, was admitted to Edgware General Hospital on March 21, 1951.

HISTORY.—Two days' generalized abdominal pain which was continuous, with exacerbations. She had vomited several times. The bowels, previously regular, had not been opened. No blood had been passed per rectum.

Past History: Appendicectomy twenty-two years previously. No other illness.

ON EXAMINATION.—T. 100; P. 120. Ill and restless. Tongue coated but moist. There was slight abdominal distension and generalized tenderness. Some faint tinkling bowel-sounds were heard.

AT OPERATION.—At laparotomy (Mr. G. R. C. Peatfield) loops of pregangrenous small intestine were found. A resection and end-to-end anastomosis was performed. The bowel affected by the thrombosis measured 36 in. (*Fig.* 585.)

PROGRESS.—Post-operative progress was uneventful and the patient left hospital on the seventeenth day. No anticoagulants were administered.

Comment.—Although no microscopical examination was made, it seems probable that this was a case of primary venous mesenteric thrombosis, since there was no evident source of an arterial embolus and no disease likely to cause either arterial or venous thrombosis. At this patient's age, however, the possibility that atheroma may have caused arterial thrombosis cannot be excluded.

Case 2 (author's case).—H. R. T., male, aged 58 years, was admitted to Edgware General Hospital on June 6, 1954.

HISTORY.—Twelve hours before admission he was seized with sudden abdominal pain which started centrally and soon became generalized. It continued without intermission. Vomiting occurred twice at the onset. The bowels had not been opened for 24 hours, and no blood had been passed per rectum. There was no history of any previous illness.

ON EXAMINATION.—T. 97; P. 80; B.P. 190/110. The patient looked pale and ill. He was groaning with

pain and lying with his legs drawn up. The tongue was dry and furred.

There was muscle guarding all over the abdomen, with marked rigidity in the epigastrium. There was general tenderness which was maximal in the right upper quadrant. No abnormality was found on rectal examination.

FIG. 585.—*Case* 1. Photograph of operation specimen.

FIG. 587.—*Case* 2. Photomicrograph of section of mesentery, showing the edge of a thrombosed vein above and to the right and two arteries below and to the left which show hyperplastic sclerosis but are not occluded.

AT OPERATION.—Under general anæsthesia the abdomen was opened through a right paramedian incision. There was a moderate amount of blood-stained free fluid in the peritoneal cavity. Coils of the distal ileum were distended and gangrenous. A resection and end-to-end anastomosis was performed. THE SPECIMEN (*Fig.* 586) was 3 ft. 9 in. long, and 2 ft. 6 in. of this was gangrenous.

Microscopical examination (*Fig.* 587) showed thrombosis of the mesenteric veins. The arteries showed hyperplastic sclerosis but were not occluded.

PROGRESS.—No anticoagulants were administered post-operatively. The patient made an uninterrupted recovery and left hospital on the sixteenth day. He has remained in good health during the 16 months following operation.

Four patients died after resection—1, aged 59, of hypostatic pneumonia on the fourth day after resection of the transverse colon ; 1, aged 66, of coronary thrombosis on the second day ; and 1, aged 67, of hypostatic pneumonia on the fifth day after resection of small intestine. Post-mortem examination showed no extension of thrombosis and the suture lines were sound. One patient, aged 65, died on the fifth day after a resection of small intestine and post-mortem examination showed that there had been further thrombosis causing infarction of the remaining 12 in. of the ileum below the anastomosis.

FIG. 586.—*Case* 2. Photograph of operation specimen.

SUMMARY

Thirty-two cases of mesenteric vascular occlusion admitted to Edgware General Hospital during the past twenty-two years are reviewed. Nineteen patients treated without operation all died. Of 7 patients who had a simple laparotomy, 1 survived. Of 6 patients on whom a resection was performed, 2 survived. Of the other 4, only 1 was found at post-mortem examination to have had a further infarction of the bowel.

I am indebted to Mr. D. B. Craig for permission to report *Case* 1 ; to Dr. J. L. Hamilton-Paterson for the microscopy ; to Miss H. Ridge, M.A., for help in searching the records ; and to Miss M. H. Shaw, A.I.D.P., for the photographs.

REFERENCES

BINTCLIFFE, E. W. (1947), *Brit. med. J.*, **1**, 50.
BROWN, M. J. (1940), *Amer. J. Surg.*, **49**, 242.
MAINGOT, R. (1955), *Abdominal Operations*, 3rd ed., 1178.
MOORE, T. (1941), *Brit. J. Surg.*, **28**, 347.

INTESTINAL OBSTRUCTION BY GALL-STONES

A REVIEW OF 179 CASES

By J. G. BROCKIS and M. C. GILBERT

CARDIFF ROYAL INFIRMARY

It is nearly thirty years since a classical paper was published by G. Grey Turner (1927), entitled "Gall Stone Ileus—A Pitfall for the Practitioner", and still the problems of this illness have not been completely solved. The text-books give a mortality for the condition between 40 and 50 per cent. If still correct, this can hardly be considered to be satisfactory, particularly in view of improvements in the treatment of intestinal obstruction. In order to investigate the present position we decided to examine the records of patients recently admitted to the Cardiff Royal Infirmary and to review some of the literature.

The causes blamed for the high mortality are late diagnosis and the advanced age of the patients. From the present inquiry these findings can be supported; frequently patients are admitted to hospital in a weak state after several days' illness and, before a firm diagnosis is made, further delay may occur owing to a failure to recognize the syndrome produced by this type of obstruction. Other factors which contribute to the high death-rate are discussed below.

Age and Sex.—The combined statistics show that for 1 man, 7 women suffer from the disease. This compares with the incidence of cholecystitis which is usually given as 1 to 8.

Table I shows that the common age for the disease is between 60 and 80 years, but there are recorded cases in comparatively young patients.

Incidence.—As a cause of intestinal obstruction gall-stones are usually disregarded as a rarity and this may well have a bearing on the failure to diagnose the condition before operation. While it is not claimed to be very common, its incidence is frequently minimized by the way in which the statistics are presented. The figure given by Vick (1932) is 2 per cent of all cases of intestinal obstruction, but this is misleading when facing a diagnostic problem. *Table II* shows a different approach, which, while simplified, does attempt to relate figures to practical considerations rather than to massive totals. Intestinal obstruction by a gall-stone is characteristically a small-gut obstruction, uncomplicated by strangulation and occurring in women of advanced years. According to Vick's figures no fewer than 23·7 per cent of all small-bowel obstructions in people over 70 years of age are due to gall-stones, excluding patients suffering from strangulation obstruction. This figure takes no account of sex, and consideration of the female cases in this age group must raise the percentage considerably higher. In the earlier two decades Vick's figures give an incidence of 12 per cent.

Mortality.—*Table I* shows that there has been a decline in the mortality from gall-stone obstruction. For the period 1920–40 it was 57 per cent, while from 1940–56 it was 33 per cent. There is some evidence from the statistics that in the second period patients were being admitted to hospital earlier in the illness.

Pathology.—The pathways by which gall-stones causing intestinal obstruction reach the bowel are well known and specimens of fistulæ between the gall-bladder and other organs are to be seen in all surgical museums. The overwhelming majority of stones pass through a fistula between the gall-bladder and the intestine. The commonest is a cholecystoduodenal fistula, but connexions are described between the gall-bladder and either jejunum, colon, or stomach. Much more rarely a stone of some size has ulcerated into the duodenum from the common bile-duct. Where the biliary tract has looked normal and what appeared to be a gall-stone has been removed from the small bowel, it has been shown (Armitage, Fowweather, and Johnstone, 1950) to be an enterolith composed largely of bile-salts and bile-pigments, but developing in a diverticulum of the bowel.

The site of obstruction by a gall-stone has been found in the 132 cases in which the information was available, to be in the ileum in 72 per cent, jejunum in 17 per cent, and the remaining 11 per cent were distributed between the stomach, duodenum, colon, and rectum.

The common site of impaction in the lower ileum is unlikely to be due only to this being the narrowest part of the small bowel. It is common experience to find functioning ileum more dilated than the size of practically any gall-stone and therefore the explanation is probably to be sought in an upset to the normal physiology of the bowel rather than to any mechanical disproportion. Movement of intestinal contents along the bowel is largely by peristaltic action. The waves start in the jejunum and pass along the gut, but many fail to reach the ileum (Avery Jones, 1952). As the strength of these waves is proportional to the tone of the bowel, which is normally less in the ileum than in the jejunum, it is to be expected on these grounds alone that while the contractions in the jejunum may be adequate to propel a gall-stone onwards they may not be so in the less active ileum.

The copious vomiting, which is a characteristic of the illness, depletes the body of electrolytes, and in 4 of our patients in which this was studied preoperatively it was found that there was a marked reduction in the level of potassium in the blood-serum. The lowest was 2·5 m.Eq./l. and the highest 3·8 m.Eq./l. While symptoms are more closely related to the cell content of potassium, these figures suggest that the electrolyte imbalance is profound.

Deficiency of potassium may be associated with symptoms of asthenia and atonia and is sometimes the cause of paralytic ileus (Streeton and Ward McQuaid, 1952; Elial, Pearson, and Rawson, 1950). The

Table I.—DETAILS OF REPORTED CASES

AUTHOR	No. OF CASES	No. OF WOMEN	AGE					SITE OF OBSTRUCTION					LENGTH OF HISTORY				MORTALITY
			Under 50 yr.	50–60 yr.	60–70 yr.	70–80 yr.	Over 80 yr.	Duodenum	Jejunum	Ileum	Colon	Others	0–3 days	4–7 days	Over 7 days	Not stated	
1900–20 Barnard (1902)	13	11	3	2	6	2	0	0	2	11	0	0	1	9	2	1	8
1920–40 Grey-Turner (1927)	8	7	0	1	2	5	0	0	1	6	1	0	3	2	3	0	2
Grey-Turner (1932)	1	0	0	0	0	0	1	0	0	0	1	0	Not stated				0
Vick (1932)	47	Not stated	6	13	14	14	0	Not stated					Not stated				33
Wakeley and Willway (1935)	11	11	1	2	2	5	1	0	2	9	0	0	6	3	0	2	3
Balch (1938)	17	16	3	1	4	7	2	0	2	15	0	0	7	6	4	0	10
Dulin and Peterson (1939)	9	8	2	4	1	2	0	2	1	6	0	0	1	3	4	1	5
McQueeney (1939)	1	1	0	0	1	0	0	0	0	1	0	0	0	0	1	0	1
Total	94	43*	12	21	24	33	4	2*	6*	37*	2*	0	17*	14*	12*	3*	54
1940 Onwards Rigler and others (1941)	2	2	0	0	1	1	0	0	0	2	0	0	1	1	0	0	0
Foss and Summers (1942)	10	7	1	1	5	3	0	0	0	8	0	2	6	2	2	0	5
Hand and Gilmore (1945)	3	3	0	1	2	0	0	0	3	0	1	0	Not stated				0
Lee (1945)	1	1	0	0	0	0	1	0	0	2	0	0	1	0	0	0	0
Mayo and Brown (1949)	3	3	0	1	2	0	0	0	1	2	0	0	Not stated				3
Denneen and Broderick (1950)	10	9	1	1	5	3	0	1	2	7	0	0	5	3	2	0	4
McLaughlin and Rains (1951)	5	3	0	0	2	2	1	0	0	3	1	1	Not stated				0
Nemir (1952)	8	8	0	0	4	3	1	0	4	4	0	0	0	5	3	0	1
Shore, Jacob, and Cannon (1953)	6	6	0	0	1	4	1	0	4	4	1	0	1	1	4	0	2
Stanistreet (1953)	5	4	0	2	2	1	0	0	0	4	1	0	4	1	0	0	3
Janes (1953)	1	1	0	0	1	0	0	0	0	2	0	0	0	1	0	0	0
Morlock, Shocket, and Remine (1956)	6	5	0	0	3	3	0	1	0	3	0	2	1	2	3	0	1
Present series	12	12	0	0	5	5	2	1	2	8	0	1	4	5	3	0	5
Total	72	64	2	6	33	25	6	3	16	49	4	6	23	21	17	0	24

* Vick's cases not stated (i.e., out of 47 cases only).

effectiveness of peristalsis in the bowel is determined, as stated above, by the tone of the musculature, and it may be therefore that the loss of electrolytes, and potassium in particular, is also a factor in the delay in passage of the stone through the bowel. This lowering of the general tone of the intestinal musculature is not necessarily inconsistent with the observation that a gall-stone is usually gripped by muscular spasm as the local irritation is intense enough to cause this, irrespective of the activity of the rest of the bowel, which, judging from the bowel sounds in these patients, is usually slight.

Table II.—CAUSES OF SMALL-BOWEL OBSTRUCTION WITHOUT STRANGULATION OVER 50 YEARS OF AGE (*Extracted from Vick*, 1932.)

CAUSE	50-60 YR.	60-70 YR.	OVER 70 YR.	TOTAL
Foreign body	1			1
Enterolith		1	1	2
Carcinoma	6	5	6	17
Cicatricial obstruction	6	4	2	12
Adhesions	69	54	24	147
Compression by tumour	8	4	2	14
Idiopathic intussusception	1	2	1	4
Intussusception with tumour	7	1	3	11
Volvulus	17	10	6	33
Gall-stone	13	14	14	41
Percentage due to gall-stones	10·1	14·5	23·7	14·5

CASE REPORTS

Case 1.—Mrs. B. M. D., aged 75 years.

Admitted with a history of vomiting and left-sided colicky pain for five days which would come and go but never completely disappear. During this time her bowels acted only slightly but more than once. She suffered from habitual constipation and this did not therefore surprise her.

On examination she was dehydrated and there was abdominal distension superimposed on a general obesity. The bowel-sounds were present. An enema gave a small fæcal result. As the patient refused operation, she was given intravenous fluids and the stomach emptied by suction. There was improvement in the general condition, but the pain continued with lessened severity. Three days later she was persuaded to undergo an operation, when a gall-stone was removed from the terminal ileum.

Convalescence was uneventful, but three months later she had a similar attack lasting 24 hours which was thought to be due to the passage of a second stone. There was no previous history of gall-bladder disease in this case.

Case 2.—Mrs. M. A. P., aged 77 years.

Admitted with a twelve-day history of vomiting and abdominal pain. The vomiting was described as coming in gushes. The bowels had not acted for ten days apart from a slight action with several enemas. She gave no previous history of gall-bladder trouble, but had received treatment for myxœdema.

On physical examination the patient was noted to be obese and there appeared to be some abdominal distension with definite tenderness in the right hypochondrium. Bowel-sounds were present but not increased. Radiography showed the presence of fluid levels in the small intestine, but no stone was seen. The serum-electrolytes were as follows: Na 160 m.Eq./l., K. 2·5 m.Eq./l., NaCl 80 m.Eq./l., CO_2 21 m.Eq./l.

Laparotomy revealed an obstruction of the terminal ileum by a gall-stone, which was removed. The patient died on the fourth post-operative day having been stuporose from the time of the operation.

Case 3.—Mrs. M. A. P., aged 77 years.

Admitted to hospital with a history of seven hours' acute colicky abdominal pain centred around the umbilicus and associated with vomiting. The bowels had acted normally four hours previously. There was no previous history of jaundice or dyspepsia.

On examination some central abdominal distension was present and X-ray examination revealed fluid levels in the gut but no opacity which would suggest a stone.

Laparotomy showed a gall-stone in the terminal ileum which could be moved proximally but not distally before removal. Convalescence was uneventful.

Case 4.—Mrs. M. J., aged 65 years.

This patient was first admitted to hospital five months before the final illness. At that time she gave a four-months' history of shivering attacks, vomiting, and upper abdominal pain. There was a palpable mass, thought to be the gall-bladder, which disappeared after treatment with antibiotics. She was sent home to await further treatment. Readmission was as an emergency, when she said that she had been vomiting for the previous ten days and that she had had diarrhœa for the previous week. During the last thirty-six hours abdominal pain had been getting progressively worse.

On examination there was some abdominal distension and marked tenderness in the right hypochondrium. The bowel-sounds were active. The patient's condition was poor and, in spite of intravenous fluids, operation was not possible. A radiograph showed fluid levels in the small intestine but no stone. She died within a few hours of admission. At post-mortem examination there was a gall-stone impacted in the ileocæcal valve.

Case 5.—Mrs. E. P., aged 66 years.

This patient gave a history of vomiting and abdominal colic of two days' duration. At the beginning of the illness the bowels were loose. An enema was given at home with a good result and a small bowel motion was passed shortly after admission. She gave no previous history of gall-bladder disease.

On examination there was no abdominal distension or tenderness. The tongue was dry and there was other evidence of dehydration. The bowel-sounds were increased. At laparotomy a stone was found 2 in. from the ileocæcal valve. It was gripped by the bowel and had to be extracted by a longitudinal incision.

Convalescence was uneventful.

Case 6.—Mrs. E. D., aged 69 years.

Admitted to hospital with a history of vomiting and upper abdominal pain of one week's duration. She said that she had vomited a little every day, but that for the twenty hours before operation it had been worse and associated with a pain in the right iliac fossa. There was also a generalized abdominal pain. Shortly after admission all pain ceased. Two large gall-stones which had been seen previously on a radiograph had disappeared when laparotomy was performed. The gall-bladder was empty, though a fistula was present into the first part of the duodenum. The cholecystostomy wound drained for a while but healed spontaneously. This patient also suffered from diabetes mellitus.

Case 7.—Mrs. S. M. S., aged 64 years.

Admitted as an emergency with a history of five-days' abdominal colic and vomiting, though the latter had

ceased for two days when the patient was first seen. The bowels had been constipated for a week but two days before she recalled having passed flatus. Abdominal distension was present and a radiograph of the abdomen showed fluid levels in the small intestine, but there was no opacity to indicate the presence of a stone. At laparotomy a gall-stone was removed from the lower ileum. The post-operative course was complicated by sepsis in the wound.

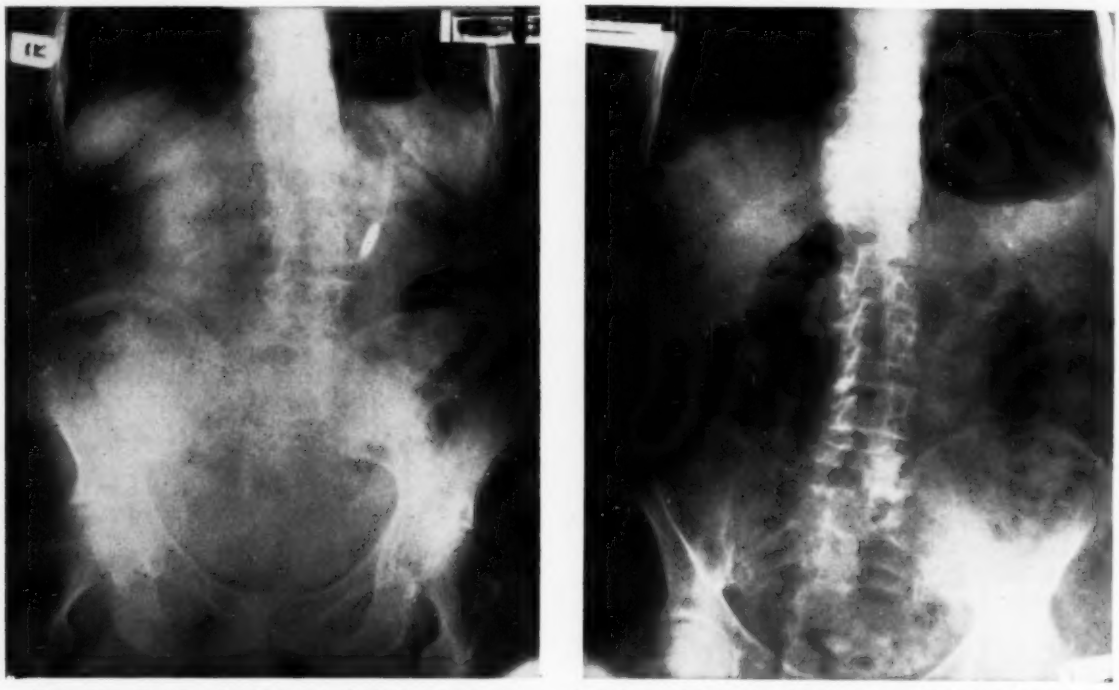


FIG. 588.—*Case* 8. Straight abdominal films in the erect and supine positions, showing absence of fluid levels in the early stages of intestinal obstruction due to gall-stones.

Case 8.—Mrs. E. E. L., aged 80 years.

Admitted to hospital with a history of intermittent abdominal pain which was generalized but of maximum intensity in the left lower abdomen and passed through to the back in the sacral region. This pain was accompanied by copious vomiting and constipation. The patient gave a history of suffering from constipation for months. She had been bedridden for some time on account of arthritis and bronchitis.

There was no abdominal distension, but vomiting took place during the examination. The radiographs, while showing some gas, probably in the small intestine, did not demonstrate fluid levels (*Fig.* 588). An enema gave a good result. The stomach contents were aspirated and a large quantity of bile-stained fluid removed. She was also given intravenous fluids. The next day she appeared better and as the aspirations had become small the tube was removed. Another enema gave a fair fæcal result. On the third day the vomiting returned in full force and by now was fæcal smelling. Laparotomy revealed a gall-stone in the lower jejunum. Progress was good following this operation, at which it was noted that there were two more large stones in the gall-bladder. By the fifth post-operative day she was getting along well, though there was some wound sepsis. On the sixth day, however, she started to vomit without having much abdominal pain. Further radiographs of the abdomen were taken and they were found to have a similar appearance to those taken before operation.

Although there was no definite proof that a further obstruction had occurred, this seemed likely and the abdomen was re-explored. A second stone was removed from the jejunum. This operation proved too much for her and she developed bronchopneumonia, from which she died. At post-mortem examination the third stone was recovered from the gall-bladder. A fistula was demonstrated between the gall-bladder and the duodenum.

The serum-electrolytes on admission were as follows: Sodium 124 m.Eq./l., Potassium 3·8 m.Eq./l., Chloride 81 m.Eq./l., Carbon dioxide 31 m.Eq./l.

Case 9.—Mrs. J. E. G., aged 70 years.

When taken to hospital this patient said she had suffered three days' continuous pain and unremitting vomiting. During the previous fifty years she had vomited after eating fatty foods but never in this way.

On examination she was dehydrated and had slight tenderness in the epigastrium. There were no other abnormalities noted. A diagnosis of pyloric stenosis was made and the stomach washed out. Intravenous fluids were given. After three days on this régime it was clear that nothing was passing along the bowel as the aspirations of the gastric contents remained considerable. Operation was decided on and was carried out ten days from the onset of the illness. A gall-stone was found in the second part of the duodenum. It was milked round to the duodenojejunal flexure and extracted there. The patient died four days later. A post-mortem examination failed to reveal a definite cause and death was attributed to primary cardiac failure.

Case 10.—Mrs. L. T., aged 66 years.

Three months prior to admission she had an attack of right-sided upper abdominal pain associated with vomiting, which her doctor diagnosed as cholecystitis. Four days before being seen in hospital she began to vomit once more. This improved one day and then became worse again the next. The vomiting was associated with colicky abdominal pain and tenderness in the left hypochondrium. In the vomit a little blood was seen.

The patient was very fat but the abdomen did not seem to be unduly distended. For five days she was

treated on intravenous fluids with only temporary improvement. A radiograph showed fluid levels in the small intestine, but no other abnormality. The bowel-sounds were not increased. Laparotomy revealed a stone 2 ft. from the ileocæcal valve. It was milked proximally and then extracted. The post-operative course was marred by wound sepsis.

Case 11.—Mrs. M. D., aged 82 years.

Admitted to hospital with a history of three days' vomiting associated with constipation. At the same time she had developed abdominal pain centred in the epigastrium and also in the left iliac fossa. Her previous history was of good health apart from the insidious onset of diabetes mellitus.

Her general condition was poor and she was dehydrated. The vomit consisted of fæcal-smelling fluid. After treatment with intravenous fluids a laparotomy was carried out. This revealed a gall-stone in the terminal ileum. Unfortunately she died forty-eight hours later. Post-mortem examination showed death to be due to bronchopneumonia following inhalation of vomit. A cholecystoduodenal fistula was present.

Case 12.—Mrs. P. B., aged 72 years.

This patient's history was of epigastric pain associated with frequent vomiting for twenty-four hours. The pain was of a colicky nature and was made much worse by eating or drinking. Previous to the onset of this illness she had suffered for some time from epigastric discomfort which was relieved by sodium bicarbonate. She also had an operation previously for a strangulated hernia.

On examination she was obese and there was marked epigastric tenderness. X-ray examination showed gas in the biliary tree and a few fluid levels in the small intestine. At laparotomy a gall-stone was found 3 ft. along the jejunum. The stone was removed after milking it along the bowel. Convalescence was complicated by wound sepsis.

DIAGNOSIS

The subjects of gall-stone ileus are in our experience nearly all obese elderly women who have had either no previous gall-bladder trouble or admit to dyspepsia only after close questioning. A history of jaundice is rare. A few are diabetics and they may, in view of their age, have organic heart disease.

The onset of obstruction by a gall-stone is heralded by vomiting. This is frequent and bile-stained at first, when the stone is lying in the duodenum. Abdominal colic follows, and is associated with the frequent regurgitation of small amounts of greenish fluid. Some time after the onset the symptoms lessen and may disappear for some hours. This can occur more than once and is probably due to the stone moving along the bowel before becoming finally impacted. Later the pain and vomiting return and the colour of the vomit changes from green to brown. These symptoms may have been present for a week or more when the patient is admitted to hospital. The pain may be described as a cramp and may be referred to either iliac fossa. As colic is usually associated in the minds of patients with constipation, a purgative has often been taken. At the onset of the illness, instead of absolute constipation, the attack may begin with diarrhœa. More frequently a history of a small motion being passed is given or of good results to repeated enemata.

Another classical feature of intestinal obstruction—abdominal distension—is usually absent, or if present may be masked by the obesity of the patient. Only when the gall-stone has become fixed in the terminal ileum for some time is distension noticeable. In a number of the reported series the stone had become impacted at a higher level. On abdominal examination one might reasonably expect to feel a tender mass in the gall-bladder area, but curiously it is the exception to find anything abnormal.

What, then, are the criteria whereby this condition may be more readily recognized and how does it differ from other forms of small-bowel obstruction? Adhesions, bands, and tumours or any other of the usual causes have in common that, once established, the obstruction remains at the same level throughout the illness. Obstruction due to a gall-stone, however, is characterized by a changing level of block starting in the duodenum and upper jejunum and progressing at intervals usually to the lower ileum. Thus it is that vomiting is prominent early and distension may be absent or of very late onset; thus also the bowel actions may be normal for the first few days. During the remissions when the stone is passing without undue hindrance down the bowel, the patient may appear to be recovering until the stone is held up again. With each successive bout the level of obstruction is lower, until finally, when the characteristic picture of low small-bowel obstruction is seen, the chances of the patient's survival have materially decreased.

In view of the uncertainties associated with the diagnosis and the spontaneous improvements which occur as the stone moves along the small intestine, there is a tendency in elderly subjects to adopt conservative treatment with intravenous fluids and gastric suction or Miller-Abbott tube. The diminution of the amount of fluid aspirated may lead to the false belief that the obstruction has been relieved. This is particularly the case when the patient has been operated upon previously and the possibility of an obstruction by a band is entertained.

As a result there is further delay in deciding to operate, and, when a decision is finally reached, the patient is liable to be in a poor condition.

It has been suggested that the use of radiography in all cases of intestinal obstruction would help to avoid this catastrophe (Rigler, Borman, and Noble, 1941). Three X-ray signs have been described: the presence of gas in the bile-ducts, fluid levels in the intestine, and a shadow cast by the gall-stone itself. Unfortunately, none of these is seen regularly. We have looked at the X-ray films for these features and only in one of the twelve was gas seen in the biliary tree. The shadow cast by the gall-stone may be lost against the vertebral column or there may not be sufficient calcium in the stone, which is almost pure cholesterol, to make it obvious. Plain X-ray photographs in the obese do not come up to the standard of detail obtained in thinner subjects, and it is unusual to see the stone. The third radiological feature described—that of fluid levels in the small intestine—is a most valuable confirmation of the diagnosis of obstruction, but unfortunately here again patients are met whose radiographs show little or no evidence of fluid levels (*Fig.* 588). This may perhaps be due to obstruction at a high level with profuse vomiting or to an incomplete obstruction with fluid and gas leaking past the stone.

Thus the value of radiology in this condition is limited, and if the findings are negative this should not be allowed to influence the decision to operate.

TREATMENT

Treatment consists in restoration of the fluid and electrolyte balance followed by laparotomy, and this should not be delayed by the hope of a spontaneous

FIG. 589.—*Case* 8. Three gall-stones occurring in the same patient. The central one caused the original obstruction, one of the end ones a recurrent episode, and the last was found at autopsy. Note the absence of facets on the central stone, although two other large stones were present.

cure of the obstruction. Undoubtedly some patients cure themselves, and in a personal case not included in this series a gall-stone was pushed through the ileocæcal valve at operation without any difficulty and would probably have passed without operative intervention.

It is usually said that the stone should be moved away a few inches from the site of obstruction before opening the bowel. This is a counsel of perfection, as we have found that the stone is often gripped and cannot be moved at all. There is therefore no choice but to open directly on to the stone. Another suggestion (Aird, 1950) is that the stone should be crushed with a lithotrite, but the difficulty of getting the blades around the stone has led us not to use this method. After removal the stone is examined for facets as other stones may be present. As shown in the photograph (*Fig.* 589) where the central stone was the cause of the obstruction, there may be no facets seen to suggest the presence of others and therefore it is necessary gently to palpate the remainder of the small intestine and to pass a hand up to the gall-bladder area. If a large stone is felt there, it should be removed by cholecystotomy unless the condition of the patient precludes this. It has been our unhappy experience for a second stone to cause an obstruction in the immediate post-operative period and there are similar cases reported in the literature (Grey Turner, 1927; Hand and Gilmore, 1943; Foss and Summers, 1942). There is a very real danger in leaving a large stone in the gall-bladder, and while cholecystectomy might prove hazardous a small incision in the fundus of the gall-bladder with extraction of the stone and insertion of a tube can be done without greatly adding to the operation. Grey Turner, in his *Text-book of Operative Surgery*, was loth to open the gall-bladder, but the complication of a second obstruction, which incidentally is more difficult to diagnose than the first, is by no means rare and we feel fully justifies the procedure.

Wound healing in the elderly subject is frequently poor and anærobic infection of the abdominal wall not unknown. Every effort should be made to avoid soiling during the operation and it is wise to drain the rectus sheath. Five of the present series had serious wound infections and this has been described by many other authors.

SUMMARY

A series of 12 patients suffering from gall-stone obstruction of the intestine is described and the problem of reducing the mortality rate is discussed as a result of the experience gained and after reviewing the literature.

The key to a lower mortality rate must lie in earlier diagnosis, and the history of these cases and the radiographic changes are described.

Certain points in the operative technique are also mentioned and the importance of correcting the severe electrolyte imbalance which may occur.

We should like to thank the Surgical Staff of the Cardiff Royal Infirmary for permission to report these cases under their care; and Professor Lambert Rogers, Mr. A. C. Lysaght, and Mr. D. B. E. Foster for helpful criticism of this paper.

REFERENCES

AIRD, I. (1950), *Techniques in British Surgery* (ed. Maingot), 318. London: Saunders.
ARMITAGE, G., FOWWEATHER, F. S., and JOHNSTONE, A. S. (1950), *Brit. J. Surg.*, **38**, 21.
BALCH, F. G. (1938), *New Engl. J. Med.*, **218**, 457.
BARNARD, H. L. (1902), *Contributions to Abdominal Surgery*, 85. London: Arnold.
DENNEEN, E. V., and BRODERICK, T. C. (1950), *Ann. Surg.*, **131**, 225.
DULIN, J. W., and PETERSON, F. R. (1939), *Arch. Surg., Chicago*, **38**, 351.
FOSS, H. L., and SUMMERS, J. D. (1942), *Ann. Surg.*, **115**, 721.
HAND, B. H., and GILMORE, W. E. (1943), *Amer. J. Surg.*, **59**, 72.
JANES, L. (1953), *Aust. N.Z. J. Surg.*, **23**, 77.
JONES, A. (1952), *Modern Trends in Gastroenterology*, 544. London: Butterworth.
LEE, M. (1945), *Brit. med. J.*, **1**, 555.
MCLAUGHLIN, C. W., and RAINES, M. (1951), *Amer. J. Surg.*, **84**, 424.
MCQUEENEY, A. M. (1939), *Ann. Surg.*, **110**, 50.
MAYO, C. W., and BROWN, P. W. (1949), *Surgery*, **25**, 924.
MORLOCK, C. G., SHOCKET, E., and REMINE, W. H. (1956), *Gastroenterology*, **30**, 462.
NEMIR, P. (1952), *Surg. Gynec. Obstet.*, **94**, 469.
RIGLER, L. G., BORMAN, G. N., and NOBLE, J. F. (1941), *J. Amer. med. Ass.*, **117**, 1753.
SHORE, S., JACOB, H. H., and CANNON, J. A. (1953), *Arch. Surg., Chicago*, **66**, 301.
STANISTREET, R. H. (1953), *Aust. N.Z. J. Surg.*, **23**, 73.
STREETON, H. P., and WARD-MCQUAID, J. N. (1952), *Brit. med. J.*, **2**, 587.
TURNER, G. GREY (1927), *Post-Grad. med. J.*, 65.
— — (1932), *Brit. J. Surg.*, **20**, 26.
VICK, R. (1932), *Brit. med. J.*, **2**, 546.
WAKELEY, C. P. G., and WILLWAY, F. W. (1935), *Brit. J. Surg.*, **23**, 377.

THE PROBLEM OF ORAL, OROPHARYNGEAL, AND HYPOPHARYNGEAL CARCINOMA IN INDIA

By J. C. PAYMASTER

DEPARTMENT OF SURGERY, TATA MEMORIAL HOSPITAL, BOMBAY

THOSE interested in the problem of cancer in India are aware of the remarkably high incidence of malignant disease of the oral cavity and the pharynx. In the absence of accurate vital statistics it is difficult to adumbrate its exact incidence, but from the record of attendance of patients at the Tata Memorial Hospital, an institution devoted exclusively to the diagnosis and treatment of cancer and receiving cancer patients from all over India, it would appear that malignant neoplasms of the oral cavity, the oropharynx, and the hypopharynx together account for 45 per cent of all cancers; the explanation of this high incidence is not yet clear. At one time it was suggested that because of excellent facilities for radiation therapy at the Tata Memorial Hospital many more cases of oral and pharyngeal cancer were referred there for treatment, but observers from other parts of India also report a similar high frequency of oral cancer. The practice of chewing betel-nut with slaked lime and tobacco, the smoking of a cheap variety of tobacco, the consumption of a diet deficient in vitamins, poor oral and dental hygiene, and the use of irritating dentifrices have all from time to time been suggested as playing a role in the causation of this type of cancer.

During a period of ten years (1941–50) no less than 8100 cases were recorded as having malignant lesions in the oral cavity, oropharynx, and the hypopharynx out of a total of 18,000 cases of cancer. From a detailed study of this vast clinical material we have been able to make a few interesting observations, and for the purpose of this study we have taken into account only those cases in which there was definite histological evidence of malignancy. Malignant disease of the oral cavity, the oropharynx, and the hypopharynx will be considered separately.

CANCER OF THE ORAL CAVITY

In carcinoma of the oral cavity are included malignant neoplasms which arise from the lips, the buccal mucosa, the anterior two-thirds of the tongue, the upper and lower alveoli, the floor of the mouth, and the hard palate. Cancer of these structures is grouped together because it has been observed that a carcinoma developing in any one of them is a squamous-cell carcinoma, usually composed of well-differentiated cells. The rate of growth tends to be relatively slow and lymph-node metastases occur late in the progress of the disease and remain localized to one side of the neck, provided the primary disease is not advanced and has not crossed the midline. In our Tata series the deep cervical chain of lymph-nodes is less frequently affected, since the patient often becomes aware of the primary lesion himself and seeks medical aid.

In our series oral cancer amounted to 13 per cent of all cancers. Lawrence and Brezina (1945) state that carcinoma of the entire oral and pharyngeal mucous membrane constitute only 3 per cent of all cancers; Ackerman and Regato (1954) give the incidence of oral cancer as 5 per cent of all carcinomata; Hayes Martin (1949) gives the incidence of "mouth cancer" or oral cancer as 4 per cent of all human cancer, but he includes tonsils, soft palate, and the base of the tongue in this group. Lane (1953) registers the incidence of oral cancer as 8 to 10 per cent of all cancers. The disease was observed to

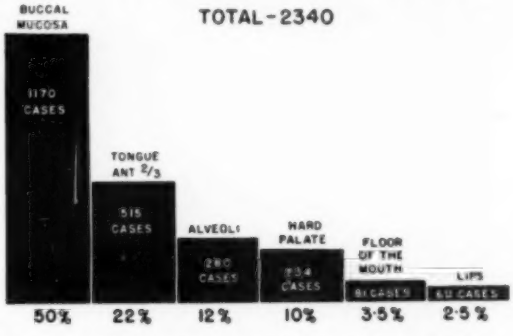


FIG. 590.—Distribution of carcinoma of the oral cavity.

occur mainly in the males, the ratio of male to female being 3 : 1. The maximum number of cases was recorded in the age group of 40–50 years.

The main communities in the State of Bombay are the Hindu, Muslim, Indian Christian, and Parsee. The male and the female members of these communities take equal advantage of the facilities offered by the Tata Memorial Hospital, and we have observed a marked difference in the distribution of cancer in the male and the female members of these communities.

Fig. 590 indicates the distribution of the disease in the oral cavity. The preponderance of the carcinoma of the buccal mucosa which accounts for 50 per cent of the oral group of cases is very striking. Pack and Le Fevre (1930) and Hayes Martin have reported the frequency of this carcinoma as 9·5 per cent of all intra-oral carcinomas: Burford and Ackerman (1945) held the frequency to be 10 per cent, which is in agreement with Richards and most observers in Western countries; but from Southern India Somerville (1944) and Khanolkar (1950) recorded a high incidence of cancer of the buccal mucosa. The habit of chewing betel-nut and betel-leaf has often been suggested as a cause for this frequency; but recently this problem was studied in detail and the conclusion reached was that the mere habit of chewing betel-leaf and betel-nut without the other ingredients was harmless. We believe, however, that when slaked lime, tobacco, and other spicy ingredients are chewed with betel-nut and kept in contact with the mucous membrane of the cheek and tongue for many hours a day the chances of development of a carcinoma are greatly increased, and we have observed the development of such cancers.

The Decani sect of Hindus is specially addicted to this habit, and the cancer of the buccal mucosa and the anterior two-thirds of the tongue has been observed to be common in them.

Carcinoma of the anterior two-thirds of the tongue came second in frequency among carcinomatous lesions of the oral cavity, accounting for 22 per cent. The incidence of this variety of cancer varies from 25 per cent to 70 per cent according to different observers: Ledlie and Harmer (1950) report the incidence as 28 per cent of " cancers of the mouth ". Lane (1953) believes it to be 35 per cent of all oral cancers: Wookey, Ash, Welsh, and Mustard (1951) found the incidence to be 40 per cent of all oral cancers, and Khanolkar (1950) regarded the incidence as amounting to 50 per cent, but he has included the base of the tongue, which is considered by most as belonging to the oropharynx. A very high incidence has been quoted by Cade (1949, 1950), almost 70 per cent of all oral cancers.

Carcinomata of the tongue and buccal mucosa are well known to develop from a pre-existing leucoplakia, and according to Hayes Martin 46 per cent of patients with carcinoma of the tongue showed co-existing leucoplakia. In our series leucoplakia was noted in only 20 per cent of the cases, though we have reasons to believe that it occurred more often than was recorded. A recent series showed that leucoplakia was present in 32 per cent of our cases.

Ackerman and Regato (1954) record a high incidence of syphilis among males with carcinoma of the tongue, and quotes an incidence as between 20 to 40 per cent, a figure approximating the experience of Levin, Kress, and Goldstein (1942), and Martin (1949). It is worth noting that the incidence of syphilis as judged from a positive serological test amounted to only 10 per cent of all our oral and pharyngeal carcinomata and could not therefore be considered an important aetiological factor in explaining the high incidence.

In a series of 5000 cases of cancer of the oral cavity observed over a period of thirty years, New and Hallberg (1941) found the incidence of carcinoma of the hard palate to be only 0·5 per cent; in our series, on the other hand, the hard palate was the seat of epidermoid carcinoma in 10 per cent of cases,

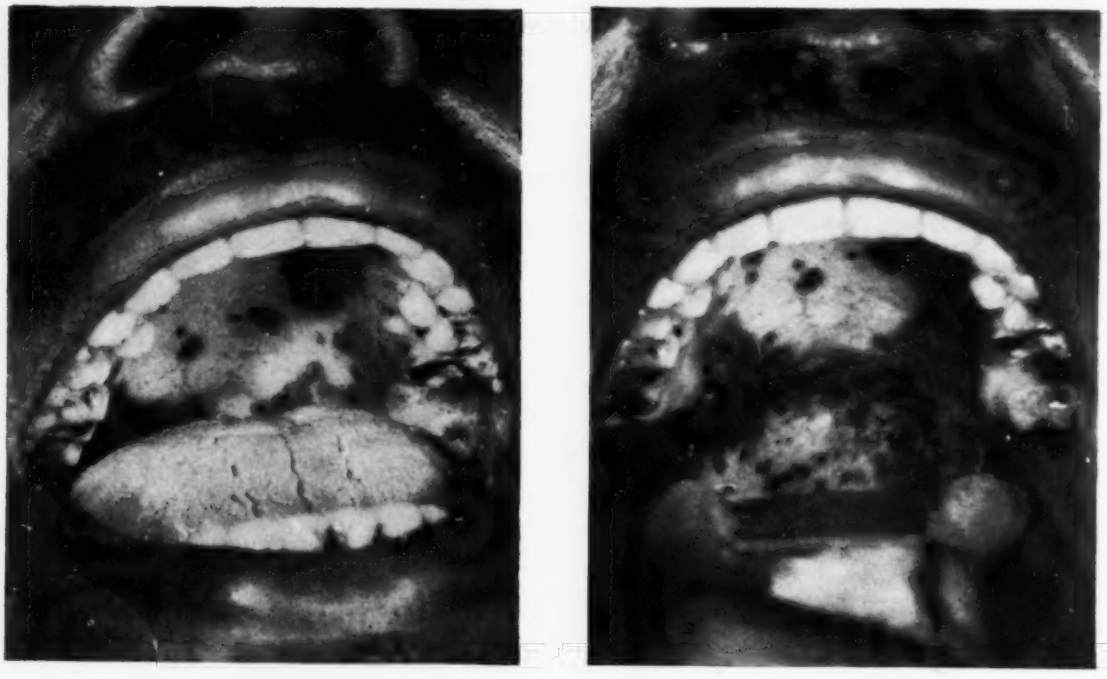


FIG. 591.—Showing patchy pigmentation of the mucous membrane of the hard and soft palates.

and in Vizagapatam, Kini, and Subba-Rao (1937) observed 52 carcinomata of the palate among 335 cases of intra-oral cancers (15 per cent). The high incidence in the Indian sub-continent may be due to irritation from the habit of smoking a cheap variety of locally made cigar called ' chutta ', which is smoked mainly by the poor by placing the lighted end inside the mouth to prevent it from ' going out ' repeatedly!

Most observers in Western countries have regarded carcinoma of the lip as a frequent form of oral cancer: Ahlbom, from the Radiumhemmet, reports a high incidence in females who suffer from Plummer-Vinson's syndrome. We are surprised at the extremely low incidence of carcinoma of the lip in our series, and the experience of observers in other parts of India has been similar, except in Uttar Pradesh and Bihar where this disease has been found to occur much more frequently. The disease invariably occurs in the lower lip and is believed to be due to the action of slaked lime and tobacco. This condition has been described as ' Khaini cancer ' by Khanolkar (1950).

In the course of our study of the oral and pharyngeal cancers we observed the following interesting clinical features. We noticed that 5 per

cent of normal healthy adults had large scattered areas of black pigmentation (accumulation of melanin) in the mucous membrane of the mouth and pharynx : more than a thousand cases were studied as controls. The presence of this type of pigmentation was found to be five times more frequent in persons suffering from oral and pharyngeal cancers than in the normal controls.

Another clinical feature noted in our series from the Tata Hospital was the presence of localized areas of dense submucous fibrosis, which was seen mainly in the soft and the hard palates and the tonsillar fossæ : less frequently this type of fibrosis was observed in the buccal mucosa ; the rest of the mucous membrane of the mouth and pharynx remained normal. (*Fig.* 591.) This type of fibrosis occurred mainly in young subjects of both sexes in whom there was no history of excessive smoking or tobacco chewing ; the only other abnormality detected was moderate anæmia. The affected areas presented a lustreless, pearly-white appearance and felt dry and tough to touch. The initial complaint was a severe burning sensation in the affected areas and inability to take spicy food. Slowly the fibrosis progresses and infiltrates the underlying muscles, leading to a gradual trismus and fixity of the soft palate. In approximately one-third of such cases we have observed a slow-growing type of squamous-celled carcinoma develop in the affected region. These cases are most difficult to treat, the trauma of surgery producing further fibrosis and increasing the deformity ; the results of radiation therapy are also disappointing.

Because of comparatively slow growth and localized metastases in oral carcinomata, it was possible to render beneficial treatment to a greater percentage of cases than in the other groups : the primary disease was treated either by radiation therapy or by surgery, the latter method being employed more often in our series, and not unnaturally with special frequency where there was involvement of the bone. Metastases in the neck were treated by a radical block dissection of the neck whenever possible. When surgery was refused or when metastases were unsuitable for surgical excision, treatment was given by means of external roentgen therapy and/or by implantation of radon seeds. The prognosis in carcinoma of the oral cavity is fair.

CANCER OF THE OROPHARYNX

Under the heading carcinoma of the oropharynx are included those malignant neoplasms which arise from the soft palate with its anterior and posterior pillars, the tonsils, the base of the tongue, including the vallecula and the lingual surface of the epiglottis, and the lateral and posterior pharyngeal walls situated between the levels of the free edge of the soft palate above and the base of the epiglottis below.

Carcinomata of the oropharynx are observed to be more malignant in nature than those of the oral cavity or the hypopharynx ; the tumours are often composed of epithelial cells which show less differentiation and hence are rapid in spread. Lympho-epithelioma is more often encountered in this anatomical site. The lymph-node metastases occur early and frequently involve the upper group of the deep cervical chain of glands, and the incidence of bilateral metastases shows increased frequency. Carcinoma of the oropharynx is best treated by radiotherapy.

Fig. 592 shows the distribution of the disease in the oropharynx.

Carcinoma of the oropharynx constitutes 20 per cent of all cancers and is one of the most frequent varieties of malignant disease met with at the Tata Memorial Hospital.

The base of the tongue was the seat of disease in 60 per cent of oropharyngeal cancers, and here

FIG. 592.—Distribution of carcinoma of the oropharynx.

the disease was found to occur either in the form of a vascular cauliflower-type of growth situated on one side of the midline or as an infiltrated fissure or crater in the glossopharyngeal sulcus, which later invaded the tongue. An early cancer in the latter site frequently eluded detection, unless a careful search was made. Ackerman considers this type of cancer as a separate entity, but we prefer to include it among the neoplasms of the base of the tongue. We had over two hundred such cases ; the disease being situated away from the midline, the metastases were strictly limited to the affected side, and hence the prognosis seemed better in this variety. In very few cases carcinoma was seen to arise in the vallecula or the central part of the base of the tongue. Cancer of the base of the tongue was more frequent in the Gujerati sect of Hindus, and in them the disease occurred more often nearer the midline than in the glossopharyngeal sulcus. The prognosis of carcinoma of the base of the tongue has been reported as poor by many observers : Baud (1950) and Windeyer (1950) have reported only a 10 per cent five-year survival rate. In a recent study of 500 unselected cases of cancer of the base of the tongue with definite histological evidence of malignancy and treated at the Tata Hospital by external roentgen therapy supplemented with radon gold seeds we found a five-year survival rate of 25 per cent. In this series there were all the histological varieties of malignant growth, including the lympho-epitheliomata.

Twenty-five per cent of malignant growths in the oropharynx were observed to originate in the tonsils. Histologically, a large proportion of these tumours were composed of less-differentiated epithelial cells, and lympho-epithelioma was the most frequent variety met with in this region. External and peroral roentgen therapy through suitable ports was the treatment of choice in our series. Mody (1944) reviewed a small series of unselected cases treated exclusively by radiation therapy and reported a five-year survival rate of 30 per cent.

Carcinomata of the soft palate were observed to be composed of fairly well-differentiated cells; yet the spread of the growth proved rapid. Most of the tumours originated near the midline, thereby increasing the chances of bilateral cervical lymph-gland metastases. The mobility of the palate may be a factor responsible for the rapid spread of this form of cancer. We relied mainly on external and peroral roentgen therapy to control the disease.

CARCINOMA OF THE HYPOPHARYNX

In the hypopharynx the malignant growths were seen to arise mainly from the following sites: The pyriform fossa was the seat of disease in a large percentage (70 per cent) of our cases. In a few others (20 per cent) the disease was observed to originate in the mucous membrane covering either the laryngeal surface of the epiglottis, the aryepiglottic folds, or the arytenoids. Carcinoma which occurs in this site is sometimes called 'carcinoma of the extrinsic larynx' or 'carcinoma of the epilarynx'. In only 10 per cent of cases was the disease observed to originate in the posterior wall of the hypopharynx or in the retrocricoid region. It must be admitted that owing to the spread of the disease it was not possible in many instances to ascertain correctly its point of origin.

Fig. 593 indicates that carcinoma was observed to develop in the pyriform fossa in upwards of 1500 cases. Malignant neoplasms in this anatomical site are treacherous, inasmuch as they progress unsuspected till metastases appear in the neck, and inasmuch as the hypopharynx is a narrow structure the cancer rapidly spreads across the midline, giving rise to bilateral cervical metastases. In our 1500 cases the cervical lymph-node metastases are recorded as involved in 75 per cent, and in 50 per cent of the latter group the lymph-nodes were involved on both sides of the neck. In almost seven hundred cases the disease originating in the pyriform fossa had spread on to the larynx or had encroached upon the retrocricoid region or the posterior wall of the hypopharynx. Since the majority of cases of carcinoma of the pyriform fossa presented themselves for treatment when they already had cervical metastases and/or when there was extension of the disease beyond the limits of the fossa, we employed as a rule external radiation therapy through multiple ports: the ports were so designed that they included the metastases along with the primary site. The prognosis of cancer in this site is poor: thus Hayes Martin and others record only 12–15 per cent of five-year survival rates, and our experience has been equally disappointing. Dissatisfied with the results of radiation therapy Morfit (1955), Raven (1954), and others have attempted surgical excision. The crux of the problem lies in early detection of this disease, which develops silently till metastases appear.

Carcinomata which arise from the mucous membrane of the epilarynx are usually slow in growth and because of their position give rise to symptoms which lead to their early detection. Unfortunately these are difficult cases to treat; situated in the central part of the hypopharynx and in close association with the laryngeal cartilage these

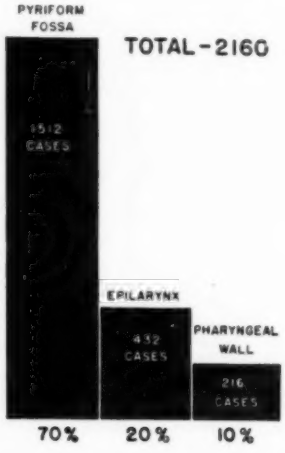


FIG. 593.— Distribution of carcinoma of the hypopharynx.

tumours tax the skill and experience of the radiotherapist in his attempt to deliver a lethal dose to the tumour. However, we have observed much better results in this type of carcinoma than in the growths originating in the pyriform fossa. The late complications of radiotherapy in this region have been radionecrosis of the cartilage and œdema of the glottis necessitating a tracheotomy for a variable length of time. In certain cases lateral pharyngotomy or pharyngolaryngectomy may be the method of choice.

SUMMARY

Carcinoma of the oral cavity, oropharynx, and the hypopharynx is extremely common in India, and we suggest that the only way to detect early lesions would be by periodical examinations of the above sites in all apparently healthy males above the age of 40 years.

Analysis of our series of 8100 cases showed that carcinoma of the oropharynx was one of the most frequent forms of cancer met with at the Tata Memorial Hospital and that the base of the tongue was the seat of disease in 60 per cent of cases in this group. The buccal mucosa was the primary site in 50 per cent of the cases of carcinoma of the oral cavity, and the pyriform fossa* was the seat of cancer in 70 per cent of carcinoma of the hypopharynx.

We have recorded our observations regarding (*a*) the presence of pigmentation in the mucosa of the oral cavity and its association with oral cancer, and (*b*) the presence of submucous fibrosis in the oral

* Carcinoma of the pyriform fossa is usually included among cases of carcinoma of the oropharynx rather than hypopharynx (*Editor*).

cavity and the subsequent development of cancer in these individuals. The role of chewing betel-nut with slaked lime and tobacco has been discussed.

REFERENCES

ACKERMAN, L. V., and REGATO, J. V. (1954), *Cancer, Diagnosis, Treatment and Prognosis*, 228. St. Louis: C. V. Mosby Co.

BAUD, J. (1950), *Amer. J. Roentgenol.*, **63**, 701.

BURFORD, W. N., and ACKERMAN, L. V. (1945), *Amer. J. Orthodont.* (Oral Surg. Sect.), **31**, 547.

CADE, S. (1949), *Malignant Disease and its Treatment by Radium*, 2nd Ed., vol. II. Bristol: Wright.

— — (1950), *Amer. J. Roentgenol.*, **63**, 716.

KHANOLKAR, V. R. (1950), *Acta Un. int. Cancr.*, **6**, 881.

— — and SURYABAI, B. (1945), *Arch. Path* (Lab. Med.), **40**, 351.

KINI, M. G., and SUBBA-RAO, K. V. (1937), *Indian M. Gaz.*, **72**, 677.

LANE, S. L. (1953), *Oral Surg.*, **6**, 258.

LAWRENCE, E. A., and BREZINA, P. S. (1945), *J. Amer. med. Ass.*, **128**, 1012.

LEDLIE, E. M., and HARMER, M. H. (1950), *Brit. J. Cancer*, **4**, 6.

LEVIN, M. L., KRESS, L. C., and GOLDSTEIN, HYMAN (1942), *N.Y. St. J. Med.*, **42**, 1737.

MARTIN, H. (1949), *A Monograph for the Physician*, 1–76. American Cancer Society, Inc.

— — MUNSTER, HILMAR, and SUGARBAKER, E. D. (1940), *Arch. Surg. Chicago*, **41**, 888.

— — and PFLUEGER, O. H. (1935), *Ibid.*, **30**, 731.

MODY, K. P. (1944), *Med. Bull.*, **12**, 109.

MORFIT, H. M. (1955), *Surgery*, **37**, 229.

NEW, G. B., and HALLBERG, O. E. (1941), *Surg. Gynec. Obstet.*, **73**, 520.

PACK, G. T., and LE FEVRE, R. G. (1930), *J. Cancer Res.*, **14**, 167.

RAVEN, R. W. (1954), *Brit. J. Surg.*, **42**, 113.

SOMERVELL, T. H. (1944), *Ibid.*, **32**, 35.

WINDEYER, B. W. (1950), *Amer. J. Roentgenol.*, **63**, 719.

WOOKEY, H., ASH, C., WELSH, W. K., and MUSTARD, R. A. (1951), *Ann. Surg.*, **134**, 529.

MUSCLE PARALYSIS IN POLIOMYELITIS*

BY W. J. W. SHARRARD

ORTHOPÆDIC SURGEON, SHEFFIELD ROYAL INFIRMARY AND CHILDREN'S HOSPITAL

MUCH of John Hunter's clinical and experimental work was concerned with subjects that would now be regarded as being the responsibility of the orthopædic surgeon. To mention but a few, his Croonian lectures on muscular motion, his experiments on the healing of tendons and on the growth of bone, and the many specimens that he collected illustrating bone and joint disease. It is not known whether Hunter ever saw a patient who had been afflicted by the paralysis of acute anterior poliomyelitis or even whether poliomyelitis existed in this country at all at that time; but, had he done so, I think that he, too, would have been fascinated by the problems that it presents.

Initial Paralysis.—The most important and the most interesting feature of the disease is the muscle paralysis and its sequelæ. In fact, the discovery of weakness or paralysis in one or more muscles in a limb may be the first certain sign that a patient is suffering from acute anterior poliomyelitis at all. The paralysis usually reaches its maximum severity within 48 hours, though it may in some cases continue to increase, or involve other limbs over the course of several days. Occasionally a second wave of paralysis may follow a week or more after the complete subsidence of the initial bout of paralysis, especially if the patient has been allowed to become ambulant too soon.

At the end of the paralytic stage, a patient may have any combination of paralysis from weakness of one or two muscles in a limb to complete quadriplegia. Fortunately for those who are extensively affected, the level of the paralysis at this time is not directly related to the degree of recovery that may ultimately occur. For instance, one limb, all of whose muscles are paralysed at the height of the acute illness, may show a return of activity in almost every muscle after 2 or 3 weeks, while the equally affected opposite limb may remain completely and permanently paralysed.

Muscle Recovery.—A convenient time at which to make a detailed assessment of the residual paralysis and paresis that bears some relation to the future state of the limbs is at the end of the fourth week, when the patient has recovered from the effects of the acute illness as such, and much or all of the pain and tenderness in muscles has subsided. In routine clinical work, no better method has been devised to record the residual power in muscles weakened by poliomyelitis than that devised by the great American orthopædic surgeon, Robert Lovett, and described by his assistant, Wright, in 1912. His system of grading of muscle power was based on the ability of a muscle to move the appropriate segment of the limb against gravity, with a force greater than gravity, or with gravity eliminated. Almost all systems of clinical testing of muscle power invented since have used this principle (Medical Research Council, 1943). I have a personal preference for inserting an additional grade into his system (*Table I*), because I so often find that I need to

Table I.—GRADES OF MUSCLE POWER USED IN MANUAL TESTING

(Modified M.R.C. Scale)

Grade 0	No contraction.
Grade 1	Flicker or trace of contraction.
Grade 2	Active movement with gravity eliminated.
Grade 3	Active movement against gravity.
Grade 4	Active movement against gravity and some resistance.
Grade 5	Active movement against gravity and considerable resistance.
Grade 6	Normal power (within the limits of manual assessment).

* Hunterian Lecture delivered at the Royal College of Surgeons of England.

record the power of a muscle which will contract against considerable resistance but which is still not strong enough to be considered as normal.

For the majority of muscles, particularly those controlling the hip, knee, shoulder, and elbow, this system is accurate and constant. But it is obvious that it cannot be applied literally in the estimation of power, for instance, in the finger flexors, and here some latitude must be allowed to the experience of the examiner. It would not be appropriate in this lecture to enter into details of the technique of muscle testing, except to say that it is not always easy to do, particularly where the patient has developed good trick movements, and it is sometimes very time consuming especially in an infant or where all four limbs have been involved. I believe that it is essential that anyone who undertakes the management of the paralysis of poliomyelitis should master the details of the method.

Apart from their use in routine clinical work, serial muscle charts can be used to study the progress of the recovery in individual muscles. Here are the results of such a study made on a group of 149 patients whose muscles I tested every two months for the first year and at six-monthly intervals for the following two years (Sharrard, 1955a). The unit of recovery was a move up from one grade to the next; for instance a muscle which was found to be acting at grade 2 at one muscle test but became grade 3 at the next examination had made one unit of recovery. The histograms shown indicate the proportion of muscles that moved up one grade between one examination and the next.

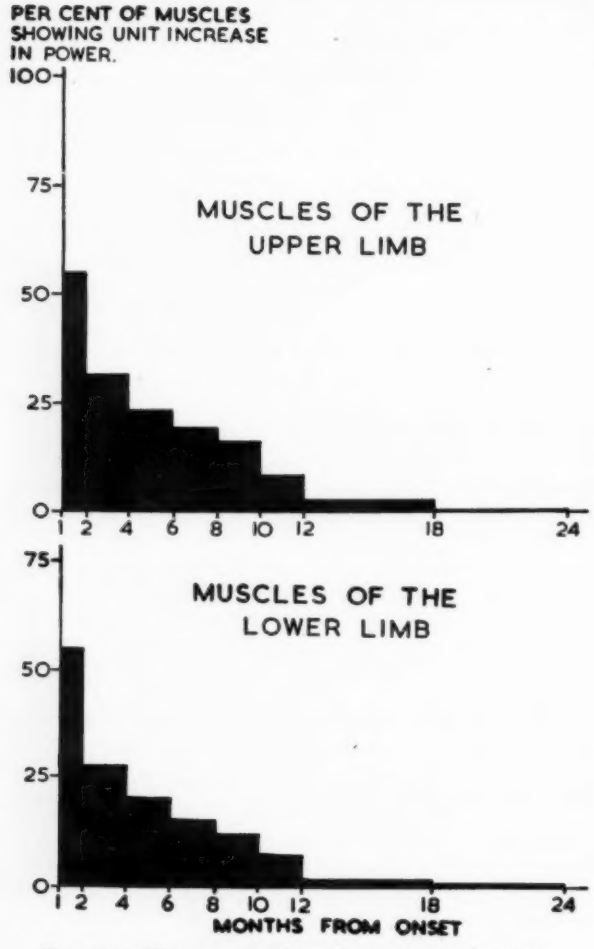


FIG. 594.—The recovery of paretic muscles in the upper and lower limbs.

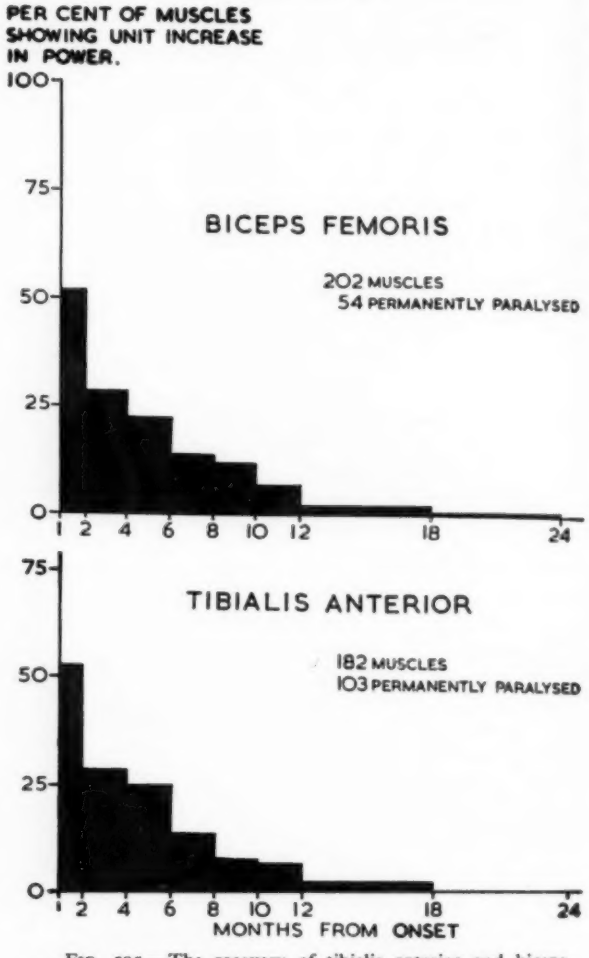


FIG. 595.—The recovery of tibialis anterior and biceps femoris. Though they are innervated at different levels in the lower limb, the course of their recovery is the same.

Recovery of Paretic Muscles.—Fig. 594 shows the recovery of muscles in the upper and lower limbs. It was rapid between the end of the first month and the end of the second, but after this the rate steadily diminished until, at the twelfth month, for practical purposes recovery ceased. A small further increase in power can result in selected muscles if they are given intensive muscle training up to the end of the second year, but it is doubtful, except in particular instances, whether this small amount of extra power is worth obtaining because it often disappears again when the training routine ceases. At the end of two years, no further recovery in any individual muscle ever occurred provided that the patient had been treated properly and that no deformity had arisen.

I want to make it clear that these results apply to the recovery of muscles and not to *functional* recovery in a limb or in a patient as a whole, which

sometimes goes on for longer than two years although the strength of individual muscles does not increase.

If the recovery of individual muscles is analysed separately, all muscles, whatever their function, size, and position in the limb, are found to recover at the same rate and to the same extent (*Fig.* 595). This is quite different from the recovery in peripheral nerve injuries, in which proximal muscles recover before distal ones as axons grow down the axon sheaths. The recovery in biceps femoris and tibialis anterior is illustrated because their different levels of innervation show that this does not occur in poliomyelitis. So, whatever the processes are that govern the recovery in poliomyelitis they must apply in the same way to every muscle and it is almost certain that recovery does *not* occur by the downgrowths of axons from the spinal cord to the periphery. The point of practical importance that derives from these findings is that, if one muscle is stronger than another in the early months of the disease, it will remain stronger throughout the period of recovery and will still be the stronger one at the end.

Recovery in Paralysed Muscles.—All the findings that I have shown to you so far have referred to paretic muscles—that is, muscles that are active however weak they may happen to be. The prognosis for recovery in completely paralysed muscles is quite different. From the earliest days of the disease a certain proportion of them are destined never to recover because they have completely lost their nerve-supply. Others have retained a number of motor nerve-cells, but for reasons which we shall consider later are temporarily out of action. *Fig.* 596 shows that, among muscles that are paralysed at the end of the first month, 68 per cent never recover, while the remainder will begin to function again with time and treatment. Among muscles that are still paralysed at the end of the fourth month, 90 per cent remain paralysed permanently, and at the end of the sixth month this figure is raised to 95 per cent. The 5 per cent that do show some recovery after this seldom achieve more than a flicker of contraction. Thus the fourth month marks the end of the period after which a completely paralysed muscle may be expected to recover any useful function.

To sum up the whole process of recovery, it is rather like the development of a negative in photography, but on a much longer time scale. During the first month the picture is quite unrecognizable; but between then and the fourth month the main outlines appear. At the fourth month you can see what the picture is, but it requires yet more time before the image becomes quite clear and the edges well defined. The picture is fully developed by the twelfth month; the patient has reached what is sometimes misnamed the 'chronic' stage of poliomyelitis and each of his affected limbs shows a permanent pattern of paralysis.

Distribution of the Permanent Paralysis.—At first sight the pattern seems to be different in every case and to be quite haphazard in its distribution; but as Lovett (1915, 1917) and Legg (1929, 1937) described, all is not quite as disorderly as it would seem to be. In the 149 patients whose recovery has been analysed above, there were over 2000 lower limb muscles that were either paralysed or paretic at the end of the period of recovery. *Table II* shows how frequently individual muscles

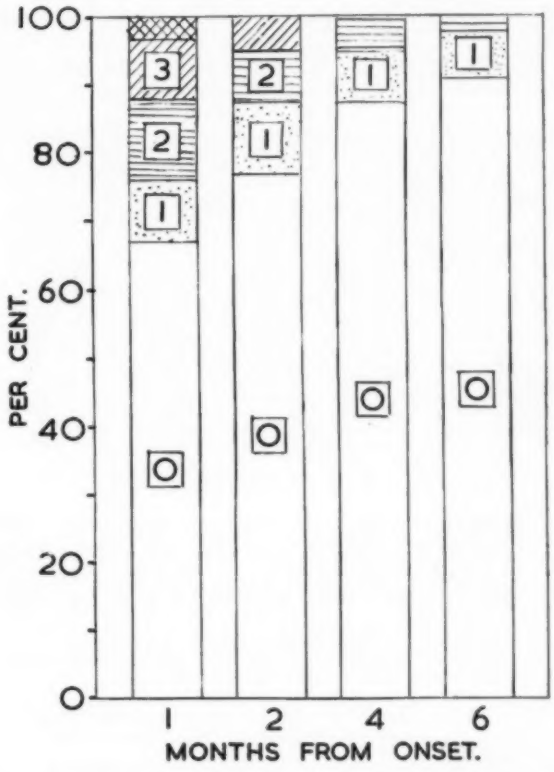


FIG. 596.—The recovery of paralysed muscles. The numerals in the columns indicate the grade of power reached at the end of two years.

were affected; the quadriceps, hip abductors, and inner hamstring muscles were often affected, the leg muscles less often and the intrinsic muscles of the foot the least frequently affected. In the same group of patients the situation of muscles that had remained permanently paralysed (*Table III*) was almost reversed. Tibialis anterior, tibialis posterior, and the long flexors and extensors of the toes led in frequency, while the hip and thigh muscles were much less often paralysed; the intrinsic muscles of

Table II.—THE FREQUENCY OF AFFECTION OF 2464 MUSCLES IN THE LOWER LIMB

Muscle	*Number Affected*
Quadriceps	184
Hip abductors (gluteus medius and minimus)	178
Inner hamstring muscles	168
Biceps femoris	164
Hip abductors	162
Hip flexors	159
Tibialis anterior	152
Tensor fasciæ latæ	149
Gluteus maximus	142
Tibialis posterior	140
Flexor hallucis longus	133
Flexor digitorum longus	130
Extensor digitorum longus	130
Calf muscles (triceps suræ)	129
Peronei	126
Extensor hallucis longus	125
Intrinsic foot muscles	93
Total	2464

the foot were, though, the least often paralysed as well as the least often affected.

If the information in these two tables is combined by determining the ratio of paralysis to paresis in each muscle, the result (*Table IV*) shows the

Table III.—THE FREQUENCY OF PARALYSIS OF MUSCLES IN THE LOWER LIMB

Muscle	*Number Paralysed*
Tibialis anterior	103
Tibialis posterior	89
Flexor digitorum longus	85
Flexor hallucis longus	84
Extensor hallucis longus	66
Extensor digitorum longus	63
Peronei	60
Calf muscles (triceps suræ)	57
Biceps femoris	54
Hip abductors (gluteus medius and minimus)	47
Quadriceps	46
Inner hamstring muscles	43
Tensor fasciæ latæ	38
Hip abductors	36
Hip flexors	34
Gluteus maximus	33
Intrinsic foot muscles	24
Total	962

susceptibility of each muscle to paralysis. The tibiales and the long flexors and extensors of the toes were very susceptible, the adductors and gluteus maximus the least. This table is the most important

Table IV.—SUSCEPTIBILITY TO PARALYSIS OF MUSCLES IN THE LOWER LIMB

Muscle	*Ratio of Paresis to Paralysis*	*Approximate Length of Motor-cell Column* (mm.)
Tibialis anterior	0·47	8
Flexor digitorum longus	0·52	8
Tibialis posterior	0·57	8
Flexor hallucis longus	0·58	8
Extensor hallucis longus	0·89	9
Extensor digitorum longus	1·06	10
Peronei	1·10	10
Calf muscles (triceps suræ)	1·26	14
Biceps femoris	2·03	14
Hip abductors	2·78	16
Intrinsic foot muscles	2·87	15
Inner hamstring muscles	2·90	20
Tensor fasciæ latæ	2·92	16
Quadriceps	3·00	22
Gluteus maximus	3·30	17
Hip adductors	3·50	22
Hip flexors	3·67	23

of the last three tables. It means that the tibialis anterior, for instance, was seven times as likely to be paralysed as the hip adductors or flexors and twice as likely to be paralysed as the peronei. These are absolute values of considerable significance and cannot be explained by the mechanism of chance.

Tables were obtained in the same way for muscles in the upper limb. In frequency of affection (*Table V*) the deltoid muscle led, followed by triceps and pectoralis major. The least affected muscles were the long flexors of the digits; the intrinsic muscles of the hand were in the intermediate position. In frequency of paralysis (*Table VI*) the deltoid muscle came second to the thenar muscles and was followed by the interossei and the triceps; pectoralis major, which was third in frequency of affection, now became twelfth.

In the table showing the susceptibility to paralysis (*Table VII*), the intrinsic muscles of the hand were the most susceptible, followed by the muscles acting on the wrist. The deltoid muscle was only moderately susceptible and the least susceptible were trapezius and pectoralis major.

Table V.—THE FREQUENCY OF AFFECTION OF 841 MUSCLES IN THE UPPER LIMB

Muscle	*Number Affected*
Deltoid	94
Triceps	85
Pectoralis major	73
Infraspinatus	68
Latissimus dorsi	63
Thenar muscles	54
Elbow flexors	53
Pronators	45
Extensores pollicis	42
Interossei and hypothenar muscles	42
Wrist flexors	42
Extensor digitorum communis	41
Wrist extensors	40
Trapezius	39
Flexores digitorum	31
Flexor pollicis longus	29
Total	841

Another curious fact that emerged from an analysis of the paralysis as a whole was the finding that certain muscles tended to be paralysed or to be spared together. Some of these associated paralyses,

Table VI.—THE FREQUENCY OF PARALYSIS IN MUSCLES IN THE UPPER LIMB

Muscle	*Number Paralysed*
Thenar muscles	28
Deltoid	25
Interossei and hypothenar muscles	15
Triceps	15
Wrist flexors	14
Infraspinatus	14
Wrist extensors	11
Pronators	11
Latissimus dorsi	11
Elbow flexors	10
Extensores pollicis	9
Pectoralis major	9
Flexor pollicis longus	8
Extensor digitorum communis	8
Flexores digitorum	5
Trapezius	2
Total	195

like that between gluteus minimus, medius, and maximus, occur between muscles of similar function and position in the limb. Tibialis anterior and posterior were very closely associated in paralysis;

Table VII.—SUSCEPTIBILITY TO PARALYSIS OF MUSCLES IN THE UPPER LIMB

Muscle	*Ratio of Paresis to Paralysis*
Thenar muscles	0·93
Interossei and hypothenar muscles	1·8
Wrist flexors	2·0
Flexor pollicis longus	2·5
Wrist extensors	2·6
Deltoid	2·8
Pronators	3·1
Extensores pollicis	3·6
Infraspinatus	3·8
Triceps	4·0
Extensor digitorum communis	4·1
Elbow flexors	4·3
Latissimus dorsi	4·7
Flexores digitorum	5·4
Pectoralis major	7·0
Trapezius	18·5

it is true that they are both invertors of the foot, but one is a flexor and the other is an extensor of the ankle.

Not all associations are between muscles of like function. One of the most surprising was that

between the calf muscles—the soleus and the two gastrocnemii—and the biceps femoris, first described by Bennett (1952). These two muscles appear to have very little in common except perhaps that they can both flex the knee, and yet if one of them is paralysed, in 9 out of 10 cases the other one is paralysed too.

It is equally surprising to find that some muscles which one would have *expected* to be associated are not; for example, the inner and outer hamstrings are *not* associated in paralysis, nor are the long flexors and the intrinsic flexors of the toes.

Patterns of Paralysis.—I would like to return now to the paralysis in individual limbs. It has often been suspected, but never proved, that patterns of paralysis exist in poliomyelitis, just as they do in peripheral nerve injuries. In a peripheral nerve lesion, each muscle in an affected limb is either completely paralysed or normal, except perhaps in some partial lesions and in root injuries. In poliomyelitis, paretic muscles of all grades of power lie side by side with paralysed and normal muscles and this makes it more difficult to discover patterns if they are present. To prove whether patterns of paralysis really were present in poliomyelitis and, if they were, to show which were common and which uncommon, I have taken a random sample of 500 limbs that had been adequately charted and studied the patterns in them.

Patterns of Paralysis in Muscles below the Knee.—These comprise 10 main groups based on the paralysis of one or more movements of the foot and ankle—that is, dorsiflexion, plantarflexion, inversion, and eversion. In each group of patterns to be described, the unbalanced pull of muscles tended to produce a particular deformity of greater or lesser degree. In growing children the deformity was often progressive as the developing bone adapted its shape; in adults, in whom this moulding of bone does not occur, the deformity was less likely to form and, when it did, progress of the deformity was limited.

GROUP I (BELOW KNEE)—TOTAL PARALYSIS

Paralysis of all muscles	74 limbs
Paralysis of all muscles except the intrinsic foot muscles	44 limbs
Deformity—None or metatarsus varus	

The first and largest group was that in which there was paralysis of all muscles below the knee or of all except the intrinsic muscles of the foot. In two-thirds of these limbs, all the muscles *above* the knee were also paralysed. The deformity was always minimal or at the most consisted of a mild metatarsus varus and flexion of the toes at the metatarso-phalangeal joints.

GROUP II (BELOW KNEE)—PARALYSIS OF INVERSION

Isolated paralysis of tibialis anterior	56 limbs
Paralysis of tibialis anterior and posterior	55 limbs
Paralysis of tibialis anterior and long toe flexors	23 limbs
Deformity—Depression of first metatarsal or valgus foot	

The second largest group includes limbs in which there was paralysis of inversion. In 56 of them the tibialis anterior was the only paralysed muscle below the knee and in 42 of these it was the only paralysed muscle in the lower limb. When there was any paralysis above the knee the quadriceps was the one affected muscle.

The deformity that resulted from an isolated paralysis of the tibialis anterior was either a depression of the head of the first metatarsal by the combined action of an overacting peroneus longus and extensor hallucis longus or a valgus forefoot; the

FIG. 597.—Valgus of the right heel and forefoot resulting from paralysis of tibialis anterior and posterior.

severity of the deformity was increased if any fixed equinus had been allowed to develop in which the forefoot was forced into even more valgus to allow the foot to be plantigrade.

When the tibialis posterior was also paralysed, a valgus heel and forefoot resulted (*Fig.* 597).

GROUP III (BELOW KNEE)—PARALYSIS OF INVERSION AND DORSIFLEXION

Paralysis of tibiales and long toe extensors	12 limbs
Paralysis of tibiales and long toe extensors and flexors	9 limbs
Deformity—Equino-valgus foot	

This group was like the previous one except that the paralysis of the long toe extensors always produced a drop foot in addition to a valgus deformity.

GROUP IV (BELOW KNEE)—PARALYSIS OF INVERSION, DORSIFLEXION, AND EVERSION

Isolated action of calf and intrinsic foot muscles	23 limbs
Isolated action of calf, long toe flexors, and intrinsic foot muscles	10 limbs
Deformity—Severe equino-varus foot	

In this group the development of a deformity was a constant feature. It does not seem to have been recognized that, in the absence of active peronei, the calf muscle is an invertor as well as a plantarflexor of the heel. A severe and intractable equino-varus deformity always develops and, in children, progresses rapidly because the tendo Achillis bowstrings on the inner side of the heel. No splint, iron, or physiotherapy will prevent this deformity.

GROUP V (BELOW KNEE)—PARALYSIS OF PLANTARFLEXION AND INVERSION

Paralysis of calf, tibiales, and long toe flexors	16 limbs
Paralysis of calf and tibiales	9 limbs
Isolated action of long toe extensors and intrinsic foot muscles	6 limbs
Isolated action of peronei and intrinsic foot muscles	14 limbs
Deformity—Calcaneo-cavo-valgus foot	

In this group the functional disability was often slight because it was associated with minimal

paralysis above the knee, but some degree of calcaneo-cavo-valgus deformity developed in every case (*Fig.* 598) in a child. The mechanism of production of this deformity is a complex one in which the ankle is hyperextended and the forefoot flexed by the

FIG. 598.—An early stage of calcaneo-cavo-valgus resulting from paralysis of plantarflexion and inversion.

combined action of the peronei and the muscles acting on the toes. Like the deformity in the last group, it is impossible to prevent its progress by any kind of conservative treatment.

GROUP VI—PARALYSIS OF PLANTARFLEXION

Isolated paralysis of the calf	8 limbs
Deformity—Calcaneo-cavus foot	

Paralysis of plantarflexion alone has been included as a separate group because it gave rise to a unique deformity of pure calcaneo-cavus. The number of limbs in this group was small because complete paralysis of the calf alone among the muscles below the knee was rare; weakness of the calf relative to the strength of the other muscles was much more common and produced a mild degree of the same deformity.

GROUP VII (BELOW KNEE)—PARALYSIS OF PLANTARFLEXION AND EVERSION

Isolated action of tibialis anterior and long toe extensors	5 limbs
Isolated action of tibialis anterior	3 limbs
Deformity—Calcaneo-cavo-varus foot	

This group was also small, but the deformity that occurred was progressive, disabling, and unsightly.

GROUP VIII (BELOW KNEE)—PARALYSIS OF EVERSION

Paralysis of peronei, long toe flexors, and extensors	3 limbs
Deformity—Severe varus foot	

Paralysis of eversion alone was rare; it is much more common in peroneal muscular atrophy with which poliomyelitis is sometimes confused. The deformity was severe and progressive.

GROUP IX (BELOW KNEE)—PARALYSIS OF INVERSION AND EVERSION

Paralysis of tibiales, peronei, and intrinsic foot muscles	8 limbs
Deformity—Cavus foot	

Deformity in the ninth group was slight because there was no lateral imbalance and it was usually limited to some degree of cavus.

GROUP X (BELOW KNEE)—PARALYSIS OF TOE FLEXORS

Isolated paralysis of the long toe flexors	6 limbs
Deformity—None	

A group included for the sake of completeness; it never gave rise to any significant disability or deformity.

In 110 limbs no muscle below the knee was completely paralysed, though many of them showed relative weakness in one or other muscles akin to one of the patterns of paralysis. The number of combinations of paralysis may perhaps make you wonder if these really are specific patterns or merely vagaries of chance.

I would remind you that there were 44 possible combinations that never occurred at all, though they should all have been present if chance had been a main factor.

Patterns of Paralysis in Muscles above the Knee.—I have stressed the relationship between deformity and paralysis below the knee because it is the deformity rather than the weakness that produces disability in this part of the limb. But in paralysis of muscles above the knee the disability is, generally speaking, proportional to the amount of the paralysis. Some movements, for instance hip or knee extension, are more important than others in causing disability. The classification of patterns above the knee is therefore based on paralysis of those movements that are likely to result in disability.

GROUP I (ABOVE KNEE)—SEVERE PARALYSES

Paralysis of all muscles	70 limbs
Isolated action of adductors	6 limbs
Isolated action of hip flexors	13 limbs
Isolated action of gluteus maximus	19 limbs
Isolated action of gluteus maximus and hamstring muscles	5 limbs
Isolated action of hip flexors and quadriceps	3 limbs
Disability—Severe or very severe	

In this, the largest group, the muscles that were acting were usually feeble and in over half the limbs the muscles below the knee were all paralysed. The rare cases in which the hip flexors and quadriceps were active in the presence of paralysis of the remaining muscles above the knee were notable for their liability to develop marked genu recurvatum.

GROUP II (ABOVE KNEE)—PARALYSIS OF KNEE EXTENSION

Isolated paralysis of the quadriceps	15 limbs
Paralysis of quadriceps and adductors	13 limbs
Disability—Slight to moderate	

In all of these limbs the paralysis below the knee was slight, there being either no muscle or only tibialis anterior paralysed. In spite of the importance that is attached by some to the action of the quadriceps as an essential muscle to stabilize and protect the knee, the loss of this muscle gave rise to surprisingly little disability and synovial effusion did not commonly occur.

GROUP III (ABOVE KNEE)—PARALYSIS OF KNEE FLEXION AND EXTENSION

Paralysis of quadriceps and inner hamstring muscles	7 limbs
Paralysis of quadriceps, inner hamstring muscles, and adductors	8 limbs
Disability—Moderate	

This group is an extension of the previous one. The disability that resulted was a little greater and a calliper was more often required to give stability.

GROUP IV (ABOVE KNEE)—PARALYSIS OF HIP FLEXION AND KNEE EXTENSION

Paralysis of hip flexors and quadriceps	5 limbs
Paralysis of hip flexors, quadriceps, and adductors	4 limbs
Paralysis of hip flexors, quadriceps, and inner hamstring muscles	5 limbs
Paralysis of hip flexors, quadriceps, adductors, and inner hamstring muscles	11 limbs
Disability—Moderate to severe	

The disability in this group was more marked than in the last two groups; a calliper had to be worn for stability unless the combined action of the calf and gluteus maximus muscles was sufficient to provide good power of extension at the knee.

GROUP V (ABOVE KNEE)—PARALYSIS OF HIP ABDUCTION AND/OR EXTENSION

Paralysis of hip adductors	7 limbs
Paralysis of hip abductors and hamstring muscles	3 limbs
Paralysis of hip abductors, hamstring muscles, and quadriceps	4 limbs
Paralysis of hip abductors, gluteus maximus, and biceps femoris	7 limbs
Isolated action of hip flexors and abductors	6 limbs
Disability—Moderately severe	

When the hip abductors alone were paralysed the disability was not great, but an ugly Trendelenburg gait was present. When all the gluteal muscles were paralysed the disability was much more severe. To maintain balance, the patient must lean forward and he is liable to develop a flexion contracture of the hip and a compensatory increase in his lumbar lordosis. If the hip flexors and adductors were strong and the small rotators of the hip were paralysed as well as the glutei, a pathological dislocation of the hip was produced in 3 cases; in each of these cases the neck of the femur had grown into valgus, as described by Blundell Jones (1954), because of the absent action of muscles attached to the greater trochanter.

GROUP VI (ABOVE KNEE)—PARALYSIS OF HIP ABDUCTION AND ADDUCTION

Paralysis of hip abductors, adductors, and quadriceps	3 limbs
Paralysis of hip abductors, adductors, and hamstring muscles	2 limbs
Disability—Moderately severe	

This small group, in which the disability was like that in Group V, was separated from it because there was no tendency to develop dislocation of the hip.

GROUP VII (ABOVE KNEE)—PARALYSIS OF HIP FLEXION AND ABDUCTION AND KNEE EXTENSION

Isolated action of gluteus maximus and adductors	1 limb
Isolated action of gluteus maximus adductors and hamstring muscles	3 limbs
Disability—Moderately severe	

These were uncommon patterns in which there was fairly marked disability and a calliper had to be used, but the presence of active extension of the hip made walking easier to achieve than in any cases in Group I.

GROUP VIII (ABOVE KNEE)—MISCELLANEOUS ISOLATED PARALYSES

Isolated paralysis of adductors	4 limbs
Isolated paralysis of biceps femoris	7 limbs
Isolated paralysis of hip flexors	3 limbs
Disability—Minimal	

This group, none of which gave rise to any significant disability, was included for the sake of completeness.

There were 265 limbs in which there was no completely paralysed muscle above the knee, though

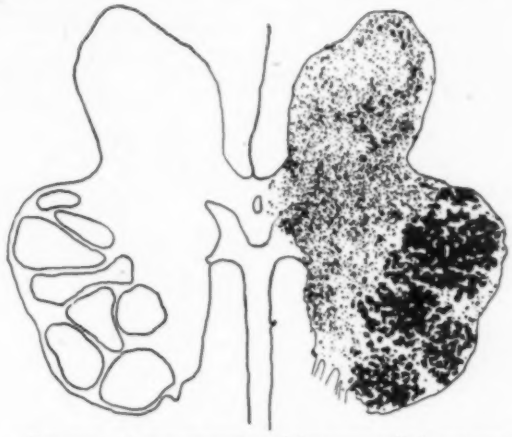


FIG. 599.—A reconstruction of the nerve-cells in 0·5 mm. of the grey matter of the first sacral segment of a normal spinal cord.

many showed weakness in some muscles, often the quadriceps or the hip abductors.

I have dealt at some length with the patterns of paralysis partly because they have never been described before to the best of my belief, and because I consider them to be as relevant to the treatment of poliomyelitis as are the patterns of motor and sensory loss in lesions of peripheral nerves. But, in peripheral nerve lesions, enough is known about their anatomy and pathology to deduce almost precisely from the clinical signs what is the site and extent of the damage. In poliomyelitis we have had to be content with knowing that the virus has attacked the anterior horn of the spinal cord somewhere in the lumbar or sacral regions. I hope to show you that these patterns and all the other clinical findings that I have mentioned can now be explained in terms of the anatomy and pathology of the spinal cord.

Motor-cell Columns of the Normal Spinal Cord.—If transverse sections of the lumbosacral cord are cut and stained to show the nerve-cells in them, the large motor cells are seen to be arranged in clusters; these aggregations of motor cells become even more apparent the thicker the section, but it is impossible to use sections as thick as one would wish. This difficulty can be overcome by projecting the images of 25 successive sections and drawing all the nerve-cells contained in them, superimposing

each image on top of the next. (Sharrard, 1953.) What then results is an accurate reconstruction of all the nerve-cells in a ½-mm. length of grey matter. The collections of motor cells in such a cell-chart (*Fig.* 599) are now much more obvious and, if you think of them in three dimensions, you will realize that they represent columns of cells running up and down the anterior horn. The small cells between

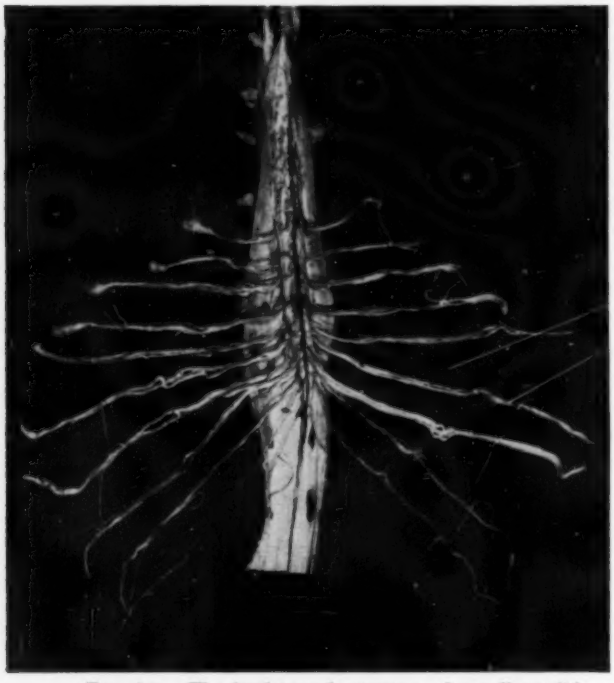


FIG. 600.—The lumbosacral segments of a poliomyelitic spinal cord obtained two years after the onset of the disease. Note the extreme atrophy of the anterior nerve-roots.

the columns and filling the intermediate region of the grey matter are the spinal interneurones.

I have used this technique to define the position and size of all the motor columns in the lumbosacral and cervical enlargements. In the lumbosacral cord a complete series amounted to about 150 cell-charts.

The topography of the motor-cell columns is remarkably constant; even if the lumbosacral plexus is prefixed or postfixed the columns move up or down the grey matter to correspond. What exactly these columns represent has been a matter of some dispute for the last fifty years. Some have said that each column represents a peripheral nerve (Marinesco, 1898, 1901), some that each represents part of a limb (Van Gehuchten and de Neeff, 1900), others that each individual muscle has its own column of cells (Sano, 1897, 1898, 1901, 1904). From my own studies of normal and pathological cords (Sharrard, 1955b), I believe that the last explanation is the correct one, though with the reservation that the columns for some muscles of similar function such as peroneus longus and brevis overlap and intermingle so that they appear as one column.

As you might guess from their root innervation, some muscles are supplied by shorter columns of cells than others. But the root-supply as a guide to the length of a muscle's column may be deceptive; the tibialis anterior is supplied from the 4th and 5th lumbar segments but the supply from the 5th segment is small and the motor-cell column is very short. Nor does the root-supply take into account differences in length of the various segments of the cord. The upper lumbar segments are more than twice as long as their numerical counterparts in the sacral segments, so that a muscle supplied by all of the 1st and 2nd lumbar segments has a column twice as long as a muscle supplied by the 1st and 2nd sacral segments.

Lesions in the Spinal Cord in Poliomyelitis.—With these facts about the normal in mind, I would now like to discuss the findings in poliomyelitic spinal cords. I was fortunate to obtain 7 cords from patients who had died more than 3 months after the onset of the acute disease, 5 of them after the end of the first year. All of them had been examined before death and records made of the power of individual muscles in their limbs.

Fig. 600 shows the spinal cord of one of these patients with the roots of the cauda equina spread out. Each anterior root is paired with the posterior root; note how thin and atrophic the anterior roots are, compared with the normal posterior roots. Serial sections were made through the whole length of the lumbosacral cord and cell-charts constructed as in the normal cords to show the number and

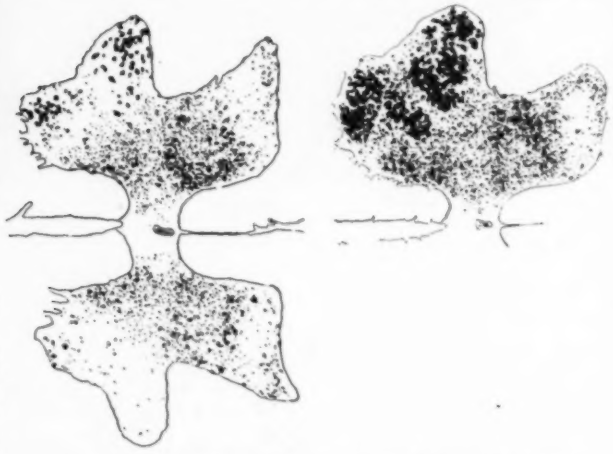


FIG. 601.—Cell-chart from the fifth lumbar segment—normal above, poliomyelitic below. In the poliomyelitic chart, the central motor-cell columns on the right side and almost all the motor nerve-cells on the left side have been destroyed.

position of residual nerve-cells in the grey matter. *Fig.* 601 shows a typical cell-chart from the 5th lumbar segment. To make it a little easier for you to appreciate the loss in abnormal charts, it is shown with the corresponding normal chart above it. I hope you can see that the central motor columns on the right side have been destroyed; the anterior and lateral columns have been thinned a bit, but about 25 per cent of their cells have remained intact. On the other side only one or two motor cells are left at the tip of the anterior part of the anterior horn.

By no means all of the cell-charts contained motor nerve-cells; in fact, a surprisingly large number did not contain any. It is of interest, and of some practical importance in the treatment of the vascular complications of poliomyelitis, to find that the cells of origin of the lumbar sympathetic are quite intact

even when all the motor cells have been destroyed, though the cells of Clarke's column are almost as susceptible as the motor cells.

By taking a complete series of cell-charts from a poliomyelitic cord a picture of the longitudinal distribution of the cell-loss can be built up (*Fig.* 602). The parts in black indicate regions of the anterior horn in which some residual motor cells remained. In *Fig.* 602 A the 1st, 2nd, and 3rd

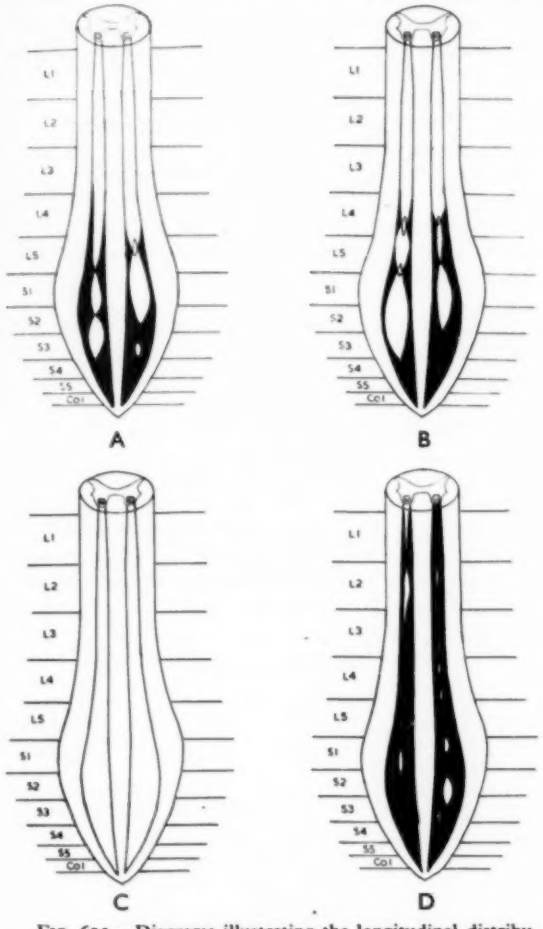


FIG. 602.—Diagrams illustrating the longitudinal distribution of the motor nerve-cell loss in four poliomyelitic spinal cords. The areas shown in black are those in which some residual motor nerve-cells were present in the anterior horn. In A and B the upper lumbar segments were devoid of cells; distal to this the destruction was focal. In C there were no motor nerve-cells. In D there were several foci of motor-cell loss in each anterior horn, but the patient had never suffered any clinically detectable paralysis.

lumbar segments in this cord were completely devoid of motor nerve-cells. Below this level, the loss occurred in foci, as if a number of small explosions of virus activity had taken place.

In *Fig.* 602 B the most intense destruction was again in the upper lumbar segments, while below that it was focal. *Fig.* 602 C shows a cord in which there were no motor cells at all on either side; this was, of course, associated with complete paralysis in both lower limbs, but I show it to emphasize the converse fact—that whenever a limb or muscle was clinically paralysed after the sixth month, there were never any nerve-cells to be found in the corresponding part of the spinal cord.

Fig. 602 D demonstrates the distribution of the cell-loss in a patient who had never suffered any paralysis in the lower limbs, even during the acute stage. In spite of this, the loss of cells taken as a whole was quite substantial—about 20 per cent—and in places up to 40 per cent of the cells supplying individual muscles had been destroyed.

Table VIII indicates how the power of a muscle is related to the percentage of residual motor nerve-cells. It will probably come as a great surprise to

Table VIII.—THE RELATIONSHIP BETWEEN MUSCLE POWER AND RESIDUAL MOTOR CELLS IN THE SPINAL CORD

Muscle Power (M.R.C. Scale)	*Percentage of Residual Motor Cells*
0	0–2
1	2–3
2	3–5
3	5–10
4	10–20
5	20–40
6	over 40

you, as it did to me, to know that a muscle of grade 3 had only between 5 and 10 per cent of its normal nerve-supply left and that with any more than 40 per cent of cells a muscle might clinically show normal power. Even if only 2 per cent of motor nerve-cells remained they were capable of demonstrating their existence by producing a contraction that could be felt in a muscle.

Correlation between Clinical and Pathological Findings.—The greater susceptibility of some muscles to complete paralysis than others is explained in the following way. The motor-cell columns of some muscles are short and of others are long; in the lumbar segments, the tibialis anterior and posterior possess short columns and are surrounded by the longer columns belonging to the quadriceps, hamstring muscles, and adductors. A small focus of poliomyelitic destruction affecting mainly the 4th lumbar segment severely damages the nuclei of the two tibialis muscles and causes them to be paralysed, while the other nuclei suffer a partial loss of their substance which, at the most, results in a mild paresis of the muscles they supply.

Thus muscles whose nuclei extend over only a short length of spinal cord are very susceptible to paralysis and muscles with long motor-cell columns are more likely to remain clinically unaffected or suffer a paresis; this correlation is shown in *Table IV*.

How may associated paralyses be explained? The curious association that I mentioned earlier between the calf muscle and the biceps femoris will serve as an example. In the nuclear representation in the spinal cord, the columns for these two muscles lie side by side and extend over approximately the same length of the cord. If one of the nuclei is completely destroyed by poliomyelitis it is very likely that the other will be destroyed also. Hence these muscles are associated in paralysis and, conversely, in freedom from paralysis. I found the same mechanism to be true for all other associated paralyses revealed by the clinical investigation.

The patterns of paralysis that I have described can be correlated with the existence of appropriate foci of destruction in the motor-cell columns of the spinal cords. If, for instance, all the motor cells in

the lumbosacral cord are destroyed except for those in the 3rd sacral segment, the common flail limb in which only the intrinsic muscles of the foot and the perineal muscles are active will result (Group I above and below the knee). A focus of destruction limited to the central part of the 2nd, 3rd, and 4th lumbar segments produces paralysis of the quadriceps and tibialis anterior (Group II above and below the knee).

Finally, a word about the mechanism of recovery. Almost everybody is agreed that there are two elements in the recovery from poliomyelitis. One is a true neurological recovery of damaged but not destroyed nerve-cells. The other is a process of compensation, adaptation, and increased efficiency in the intact neurones and muscles. The second process probably continues throughout the whole period of recovery though it assumes its greatest importance in the later months. What is not known is for how long neurological recovery can still take place. In the first 2 or 3 weeks there is plenty to explain the paralysis; everywhere in the anterior horn nerve-cells are dying or are dead and are being removed by phagocytosis. There is œdema and intense vascular change in the anterior horn so that even nerve-cells that have not been destroyed are understandably knocked out of action.

But, as Bodian has shown, within a few days cells that have been destroyed by the virus are phagocytosed. Those that remain are either normal in appearance or show central chromatolysis. By the end of the fourth or fifth week at most he found no histologically abnormal cells. This was also true of all the material that I have examined.

In all the cords taken from patients who had died *after* the fourth month the presence of motor cells always correlated with clinical evidence of activity in a corresponding muscle. Before the fourth month, though, there were several areas in which small numbers of cells that were histologically normal were present without clinical action in the muscles that they supplied.

There has been much speculation in the literature to explain why such cells should remain functionless up to this time. Almost every element in the nervous chain from the cerebral cortex to the muscle itself has been incriminated; but I see no objection to the suggestion that the nerve-cell itself and the axon which is the continuation of its substance is at fault. There is ample evidence from other regions and diseases of the nervous system—for instance head injuries—that nerve-cells may remain dormant for as long as four months. Moreover, the supporting tissues surrounding the motor cells at this time are far from fully recovered; there is still some œdema, greatly increased vascularity, and cellular infiltration.

This state of the interstitial tissues continues until at least the sixth month and sometimes longer—a fact which does not seem to have been recorded in the literature of poliomyelitis. It may well be that these changes in themselves may be sufficient to account for the continued dysfunction of the motor nerve-cells.

Application to the Management of the Paralysis of Poliomyelitis.—Of the application of all these clinical and pathological findings in the management of poliomyelitis I need say little. I hope that they will help you to know how much recovery to expect in a patient, for how long it is worth while continuing with treatment, and which paralysed muscles can be defined as incapable of recovery, so that unnecessary efforts to get them working can be avoided. I hope that you will find it possible to place a limb in its appropriate pattern of paralysis and thereby be able to anticipate deformity and minimize disability.

Finally, I hope that you will now be able to satisfy one of the basic principles of surgery that is as important to-day as it was in John Hunter's time—to know the pathology and anatomy of the condition that you are treating.

Much of the work on which this lecture was based was carried out at the Institute of Orthopædics, London.

My grateful thanks are due to its Director, Mr. H. J. Seddon, and to all the surgeons of the Royal National Orthopædic Hospital. The work was aided by grants from the National Fund for Poliomyelitis and the Medical Research Council.

I wish to thank Dr. H. Sissons and all the members of his staff for their help with the histological work and Mr. R. Whitley for his help with the illustrations.

REFERENCES

BENNETT, R. L. (1952), *Poliomyelitis*. Papers and Discussions, presented at the 2nd International Poliomyelitis Conference, p. 261. Philadelphia: J. B. Lippincott Co.
BLUNDELL JONES, G. (1954), *J. Bone Jt. Surg.*, **36B**, 375.
BODIAN, D. (1948), *Johns Hopk. Hosp. Bull.*, **83**, 1.
LEGG, A. T. (1929), *J. Amer. med. Ass.*, **92**, 31.
— — (1937), *New Eng. J. Med.*, **217**, 507.
LOVETT, R. W. (1915), *J. Amer. med. Ass.*, **64**, 2118.
— — (1917), *Ibid.*, **69**, 168.
MARINESCO, G. (1898), *Rev. neurol.*, **6**, 463.
— — (1901), *Ibid.*, **9**, 578.
MEDICAL RESEARCH COUNCIL (1943), War Memorandum. No. 7, Aids to the Investigation of Peripheral Nerve Injuries. London: H.M.S.O.
SANO, F. (1897), *Rev. neurol.*, **5**, 603.
— — (1898), *J. Neurol. Hypnol.*, **3**, 253, 274, 404.
— — (1901), *J. Neurol. Brux.*, **6**, 281.
— — (1904), *Cong. med. alienistes neurol. Pau. Annexe Rapport*, **1**, 223.
SHARRARD. W. J. W. (1953), *Proc. R. Soc. Med.*, **46**, 346.
— — (1955a), *J. Bone Jt. Surg.*, **37B**, 63.
— — (1955b), *Ibid.*, **37B**, 540.
VAN GEHUCHTEN, A., and DE NEEFF, C. (1900), *Névraxe*, **1**, 201.
WRIGHT, W. G. (1912), *Boston med. surg. J.*, **167**, 567.

OCHRONOSIS

By G. K. ROSE

CONSULTING ORTHOPÆDIC SURGEON TO THE ROBERT JONES AND AGNES HUNT ORTHOPÆDIC HOSPITAL AND THE ROYAL SALOP INFIRMARY

ALCAPTONURIA is the manifestation in an individual of failure to break down homogentisic acid, which is one of the intermediate products of tyrosine metabolism, and is presumed to be due to the hereditary deficiency of the enzymes necessary to complete this metabolism. Large quantities of homogentisic acid are therefore excreted in the urine, and this on standing, particularly when alkaline, gradually turns black. An acquired form of the disease occurs following the administration of phenol compounds, and though this is accompanied by pigmentation, it is doubtful whether the pigment in this case is identical with that in alcaptonuric ochronosis.

Marcet, in 1823, is credited with noting for the first time a substance in the urine which caused a black stain on cloth. Boedeker in 1861 named this reducing substance an 'alkapton body' and in 1866 Virchow recorded the first case of ochronosis describing the pigmentation of cartilage and other tissues. In 1891 Wolkow and Bauman determined the 'alkapton' to be homogentisic acid.

In English literature, early descriptions were by Osler in 1904 and by Pope in 1906. In 1941 Pomeranz, Friedman, and Tenick had collected 100 cases of alcaptonuric ochronosis that had been reported up to date. Their paper is of interest as it considers in detail the radiological features of this condition.

In 1932 Hogben reviewed 45 alcaptonuric families and found that the defect is usually inherited as a Mendelian recessive trait, but it was dominant in three families.

Clinically, the condition is usually recognized in childhood and frequently by the black staining of napkins. Later in life it may be discovered during routine examination of the urine for hospital or insurance purposes.

The condition is compatible with long life and there are no clinical manifestations other than the discoloration of the urine until the second or third decade when ochronosis tends to appear. The colour of the freshly voided urine is not unusual if it is acid, but if it is alkaline it appears as some variant of brown or even black. When a specimen stands exposed to air it gradually darkens at its upper surface and in time becomes black throughout. This is, of course, due to the gradual change which occurs ordinarily in urine as it stands to the alkaline side. Of interest, particularly when the appearance of the urine is normal, is that it reduces Benedict's solution, giving rise to yellow or orange precipitate and a brown or black supernatant fluid. When ferric chloride is added drop by drop to the urine an evanescent blue colour appears, and when a strong alkali is added and the specimen shaken, it promptly turns dark. All of the above reactions are presumptive evidence of alcaptonuria, but isolation of the homogentisic acid is the only certain proof.

When fully developed, ochronosis may be demonstrated by the presence of all or some of the following stigmata.

Patches of light brown or slate-grey pigment in the scleræ on either side of the corneal limbus are common, as is bluish discoloration of the external ear. The nasal cartilages and superficial muscle tendons of the hands may exhibit bluish discoloration, and brown pigmentation is seen in the skin, particularly of the face, axillary folds, thenar and hypothenar eminences, and the nails. The perspiration may be black or brown and the cerumen similarly deepened in colour.

The association of ochronosis with deforming arthritis is a very variable one. Some patients may be almost crippled at 50, whilst others may get on well into the eighties and the degree of ochronosis is not in fact directly related to the arthritic changes. In well-developed cases the spine becomes rigid with considerable deformities. Motion in the hip, knee, and shoulder joints may become very limited and painful.

On X-ray examination the presence of thinned, densely calcified, intervertebral disks is characteristic. These disks become frayed and in some instances are extruded or reabsorbed and the adjoining vertebral bodies become fused. In addition, degenerative osteoarthritic changes are apparent in the spine, lumbo-sacral, sacro-iliac, shoulder, hip, and knee joints, and calcifying deposits may be seen in tendons about the large joints. The small joints usually exhibit little or no alteration.

Clinically the patients are often, though by no means always, of reduced intelligence.

CASE REPORTS

HISTORY.—Mrs. E. W., now aged 57, was originally seen in October, 1953. She complained of pain in both hips, considerably on the right but less on the left, and stated that though the pain was maximal whilst walking, and particularly when she first started to move about, she also got pain at rest. The pain was localized rather vaguely over the whole of both legs. When she was first examined it was noticed that she was much older in appearance than her years, that she walked with an extremely poor gait with her hips in a markedly flexed position, leaning forward on to a stick. She was grossly overweight and of poor intelligence, and she lived a miserable existence, having an invalid husband who suffered from hypertension and recurrent minor strokes. Her own blood-pressure was 190/100. All movements of her spine were grossly limited and she stood with a marked pelvic tilt towards the right where she had a 1½ in. apparent shortening. The right hip was unsoundly ankylosed in a position of marked flexion and adduction, and though the position of the left hip was better, the range of movement in the joint itself was only slightly greater than the right. On both sides she also had gross osteoarthritic changes in the knees, the range on the right being 170–100°, and on the left 180–90°. She was so severely crippled that she was unable to get upstairs or put on her own shoes. She could not leave home

owing to her invalid husband and what conservative treatment that was possible in the way of a raising on her shoe on the right side and a supporting belt to her back to eliminate the part of her pain arising from this area was tried but ultimately, after the death of her husband, as she still complained of pain at rest, some operative intervention seemed to be indicated. The patient was therefore admitted to the Robert Jones and Agnes Hunt Orthopædic Hospital at Oswestry for a modified type of Girdlestone operation on the right hip using a spherical prosthesis.

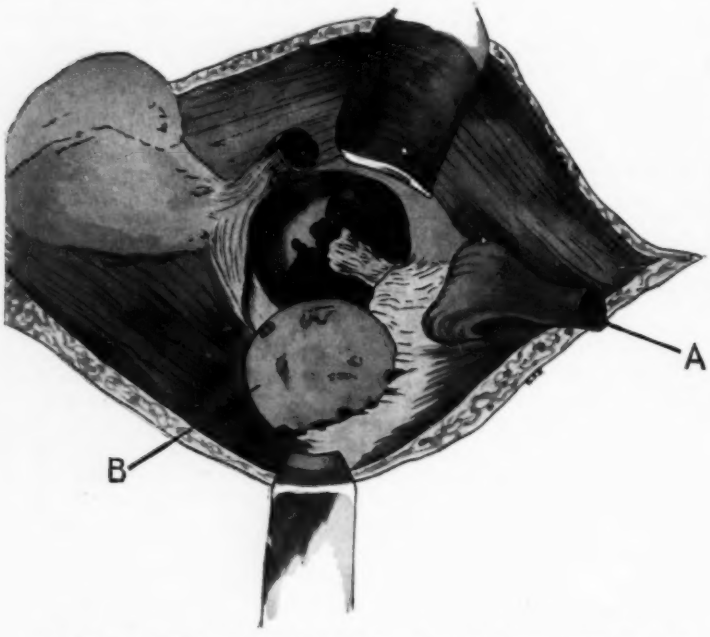


FIG. 603.—Dislocated head of the femur showing degenerative changes in the main but with little ochronotic infiltration round the margin. The inferior half of the cartilage of the acetabulum was infiltrated with ochronotic material. A, Divided rectus femoris with ochronotic tumour. B, Head of the femur.

It was noted on admission that her urine reduced Benedict's solution but it was recognized that this was a false reduction from the point of view of sugar and the true significance not appreciated. However, when operation was undertaken in August, 1954, it was noted with surprise that in the long head of the rectus femoris there was a small black tumour, about the size of a hazel nut, which when it was cut was found to be composed of coal-black material rather like damp peat in consistency. When the hip joint itself was exposed it was found that the inferior half of the cartilage was of a similar nature to the small swelling (*Fig.* 603). The operation was completed without difficulty and the material sent for section.

At this stage the significance of the urine tests became apparent and a diagnosis of alcaptonuria with ochronosis was made. Post-operatively it was shown that the urine reduced ammoniacal silver solution, gave an evanescent blue colour with ferric chloride, and the reduction with Benedict's solution left a black supernatant fluid.

Macroscopical examination of the articular tissue from the right hip showed degrees of infiltration with a jet-black material. The discoloration was most obvious in ligamentous structures, and in the remnants of articular cartilage at the rim of the osteoarthritic head of the femur. Most of the head of the femur was eburnated bone, and was not discoloured, but there was a precise black ring of cartilage round this.

Histologically, pigment was present in cartilage and ligamentous structures mostly as a diffuse staining. In the cellular areas the pigment was mostly intracellular, mainly lying within histiocytes and occasionally giant cells, but there was no chronic inflammatory reaction. The pigment did not stain with iron, fat, or silver stains and it bleached slowly with peroxide.

As stress had been placed on the hereditary metabolic nature of alcaptonuria, an endeavour was made to trace any relative of this lady. We were not helped by her low intelligence and she has apparently only one relative with whom she is on speaking terms. Although this relative, her sister, gives a history of arthritis, she steadfastly refuses to attend for examination, or even to let us have a specimen of urine, but her condition is stated not to be a serious one. She has six brothers all of whom are said to be well. Our patient had no idea that she had a lifelong abnormality in her urine.

She showed relatively few of the other clinical stigmata of alcaptonuria. She has faint blueness of the cartilage of the ears and the black spots of the conjunctivæ.

Her radiographs are, however, very characteristic indeed.

DISCUSSION

It must be extremely rare in these days for a patient to survive 57 years with alcaptonuria without the condition being discovered. From the physiologist's point of view the condition is of interest as it throws light on protein metabolism, but from the patients' point of view whilst they can be assured that the presence of homogentisic acid in their urine is benign, it must be borne in mind that deforming arthritis is a common sequel and these cases are very likely to present themselves in an orthopædic department. Although in several papers the theoretical conceptions of treatment are discussed, it is evident that no specific treatment is available and endeavours to limit the intake of proteins which will reduce the production of homogentisic acid carry greater dangers than advantages. From the orthopædic point of view, early recognition of the condition of ochronosis with appropriate advice to the patient as regards occupation and the early prevention of deformities seems to be a much more useful approach than any operative treatment can be late in the disease.

REFERENCES

BRUNE, T. (1886), *Boston med. surg. J.*, **115**, 621.
HOGBEN, L., WORALL, R., and ZIEVE, I. (1932), *Proc. R. Soc. Edin.*, **52**, 264.
OSLER, W. (1904), *Lancet*, **1**, 10.
POMERANZ, M. M., FRIEDMAN, L. J. M., and TENICK, I. S. (1941), *Radiology*, **37**, 295.
POPE, F. M. (1906), *Lancet*, **1**, 24.

PLEOMORPHIC ADENOMATA OF THE PALATE AND TONGUE

By B. BRENDAN HICKEY, KHARTOUM

PLEOMORPHIC adenomata, or mixed parotid tumours, are well known to occur in any situation other than the parotid where salivary-gland tissue is present. In the Sudan the parotid tumour appears to be relatively common. During the three-year period in which the 4 tumours to be described were removed there were received in the Stack Laboratories, Khartoum, 37 specimens of salivary tumours.

FIG. 604.—*Case* 1. Mandible.

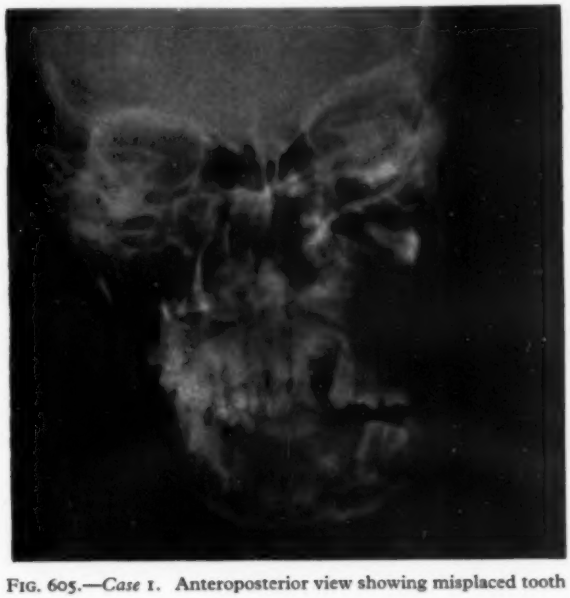


FIG. 605.—*Case* 1. Anteroposterior view showing misplaced tooth

These tumours as a whole are not uncommon in the Sudan as may be seen from the fact that during this time 69 specimens of breast carcinomata, the commonest malignant tumour, were received in the same institution. In our present state of knowledge of the causation of both tumours it is hardly profitable to speculate on the reason for this, but the facts are as recorded. The relative frequency of these tumours in other parts of Africa is commented on by Steiner (1954), who reviews a considerable literature on the subject.

CASE REPORTS

The clinical features of the four cases presented are as follows :—

Case 1.—A southern Sudanese girl of about 17 years who complained of a swelling of the palate of six years' standing which had grown slowly and was now causing difficulty in speech and mastication of solids.

ON EXAMINATION.—The patient was rather a thin girl, but she was not undernourished. She had an enormous swelling of the left side of the face resulting from a firm smooth rounded mass arising apparently from the left half of the palate, encroaching across the midline and growing downwards. There were widely separated teeth on the buccal surface. The mandible was grossly deformed on the left side, being bent outwards and thinned almost to a shell. The surface of the tumour opposite the mandible was deeply grooved by it. The backward extent of the tumour could not be ascertained, but the posterior nares were apparently blocked. The patient refused to be photographed but radiographs demonstrated the extent of the tumour and the thinned mandible (*Figs.* 604, 605) and also showed a misplaced tooth which led to speculation as to whether the mass was arising from a dental remnant.

AT OPERATION.—This was undertaken with the intention of removing the mass. Under general anæsthetic the teeth on the tumour surface were removed

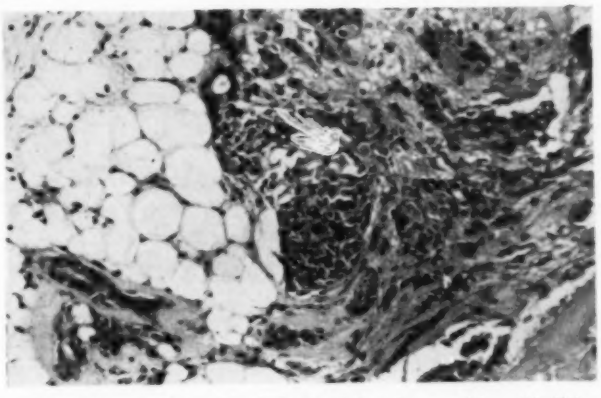


FIG. 606.—*Case* 1. Atypical glandular tissue with epithelial sprouts and fat cells incorporated in the tissue.

and the mucosa on its surface reflected upwards. It was then apparent that there was a plane of cleavage between the maxilla and the mass over which it was expanded. To gain further access the thinned maxilla was cut vertically and separated further from the tumour, which could then be moved but not extracted from its bed. The mass was then decreased in size by removing a large slice from the centre. This facilitated extraction and the whole removed with surprisingly little bleeding. A cavity lined by thinned bone in its anterior half in all directions and not communicating with either nose or maxillary sinus was left. It was then apparent that he

soft palate had been extensively stretched over the posterior half and pushed firmly against the posterior wall of the pharynx. There was sufficient redundant mucosa to close the cavity and by suturing it was possible to pull the soft palate forward to leave an adequate airway and pharyngeal opening. The patient made a good recovery, and on discharge from hospital swallowing and speech were normal.

THE SPECIMEN.—Of very firm consistency; it weighed 235 g. and measured $10 \times 7{\cdot}5 \times 7{\cdot}5$ cm. The histological appearance (*Fig.* 606) showed a pleomorphic adenoma.

Case 2.—Sudanese male, aged about 70 years, who complained of a swelling of the hard palate.

HISTORY.—The swelling had been present for about twenty years and had grown gradually and painlessly during that time. About a year ago it started to interfere with swallowing and blocked the right side of the nose. Eight months ago an operation was undertaken to remove the swelling, but it recurred three months later and has steadily increased in size.

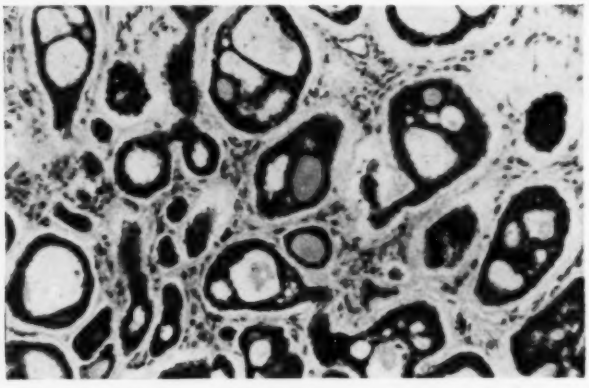


FIG. 607.—*Case* 2. Epithelial formations with cystic spaces in original tumour.

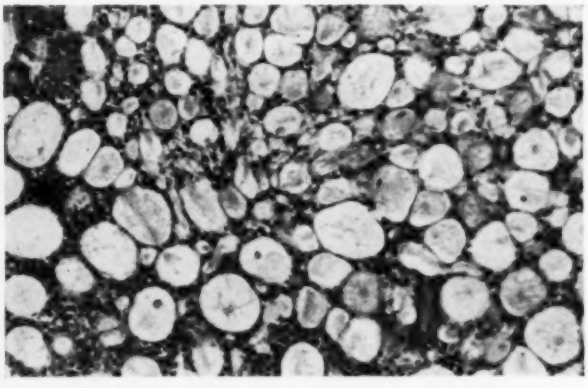


FIG. 608.—*Case* 3. Central part of tumour. Epithelial masses with cystic spaces giving cribriform appearance.

ON EXAMINATION.—A man of healthy appearance. In his mouth there was a firm irregular swelling in the posterior half of the palate measuring 5×6 cm. extending forward to the first premolar tooth, back into the soft palate and upward to the site of the maxillary sinus, encroaching upon and blocking the left side of the nose. There was a crescentic gap between the inner right border and the hard palate which had been partly removed at the previous operation. A section from the previous operation specimen was available and showed it to be a pleomorphic adenoma.

AT OPERATION.—Under general anæsthesia the left maxilla was excised, not touching the floor of the orbit, which was not encroached upon by the tumour. The operation presented no difficulty, but oozing of blood necessitated packing the cavity. The patient made a good recovery and was discharged with a well-epithelialized cavity to await the fitting of a prosthesis.

THE SPECIMEN.—The tumour measured $6 \times 5 \times 5$ cm. and weighed 56 g. Section (*Fig.* 607) demonstrated it to be a pleomorphic adenoma. Other sections taken from tissue in the rest of the maxilla showed no local spread.

Case 3.—Sudanese woman, aged about 35 years, who was admitted with a painless swelling of the posterior part of the tongue which had been present for six years and was interfering with deglutition and speech.

ON EXAMINATION.—She was a woman of healthy appearance who spoke in a muffled voice. She had a firm swelling occupying the posterior third of the tongue, chiefly on the right side. It was firm in consistency and rose so high that it touched the hard palate and extended backward. So far as could be seen the surface was not ulcerated. The mass extended forward and downward to the right submental region, where there was a visible fullness. There was limitation of protrusion of the tongue but it was not fixed. In general the mass was very ill defined.

The diagnosis was in considerable doubt. The absence of ulceration and gross fixity made a carcinoma unlikely, while negative Kham test and absence of response to vigorous antisyphilitic treatment negatived the diagnosis of gumma, considered the most likely condition on clinical grounds. Finally a biopsy of the swelling was taken from the submental region and this demonstrated a pleomorphic adenoma.

AT OPERATION.—This was undertaken in spite of the site of the tumour and its indefinite edges, as it offered the only chance of relieving the patient. Adequate access could not be obtained through the mouth alone and the method originally described by Syme was employed. An incision was made from the midpoint of the lower lip to the thyroid cartilage. The superficial structures were reflected to the right side to expose the mandible as far as the canine tooth. The muscles were detached from this part of the lower border of the mandible, the canine tooth extracted, and the bone sawn across. By this method excellent exposure was obtained and the tumour dissected out. It extended anteriorly across the midline into the left infrahyoid region; on the right side it occupied the whole of the floor of the mouth and submaxillary area; posteriorly it extended across the midline in the posterior third of the tongue, and below to the root of the epiglottis. There was evidence of infiltration around most of the periphery of the tumour and the dissection was made as extensive as possible, leaving only part of the left anterior two-thirds of the tongue attached by a few muscle-fibres

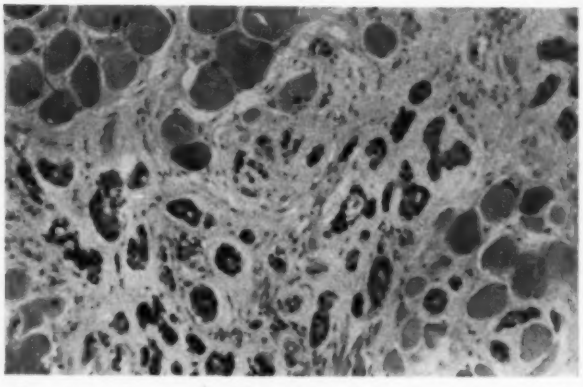


FIG. 609.—*Case* 3. Outlying part of tumour showing atypical glandular tissue lying between striped muscle-fibres.

of the hypoglossus and the hypoglossal nerve and lingual artery. Reconstruction of the oropharynx with remains of mucosa was partly effected and a tracheotomy established. The mandible was wired together but not splinted to the maxilla, as it was considered essential for the patient to be able to open her mouth.

She made a good recovery. She was able to swallow fluids in forty-eight hours and the tracheotomy was closed after seven days. The mouth healed rapidly and the remnant of the tongue functioned well for speech and mastication. The mandible was splinted to the maxilla at a later date by Mr. H. Burns Jones, dental surgeon Sudan Medical Service, and healing took place rapidly. The portions of the tumour removed weighed 83 g. and their histological appearance was the same as that of the biopsy fragment (*Fig.* 608). Invasion of the tongue muscles was seen at the periphery (*Fig.* 609).

Case 4.—Sudanese woman, aged about 40 years, who complained of a painless swelling at the back of the throat which had been present for the past five years, gradually enlarging and interfering with swallowing.

ON EXAMINATION.—She was a healthy-looking woman who presented a firm regular non-tender ovoid swelling of the soft palate (*Fig.* 610). It appeared to block off

FIG. 610.—*Case* 4. Tumour of soft palate.

the nasopharynx completely. The structures of the soft palate were stretched over it and the uvula could not be seen. A diagnosis of salivary tumour of the palate was made and it was decided to remove it.

AT OPERATION.—Under general anæsthesia the mouth was examined. The mass appeared to be tightly jammed in the nasopharynx and could not be pulled forward. An incision was therefore made horizontally over the mucosa covering it, which was then reflected. After this it was found possible to enucleate the mass from its bed and remove it. A cavity was left consisting largely of thinned-out soft palate bounded anteriorly by indented hard palate. To minimize the chances of recurrence an adequate margin of tissue was dissected away. Brisk hæmorrhage occurred from the right greater palatine artery which had to be controlled by a pack which was left stitched in position for two days.

The patient made a good recovery, the palate though considerably scarred functioning apparently normally.

The tissue on section was a typical pleomorphic adenoma (*Fig.* 611).

CLINICAL FEATURES

All these tumours were slow growing and quite painless, the maximum length of history being twenty years. They showed a tendency to grow backward into the pharynx, as shown by the fact that in three of the four cases (*Cases* 1, 3, and 4) it was impossible to assess the backward spread until the patient was anæsthetized, and they all interfered to some extent with deglutition. This may be explained by the fact that they all arose in the posterior part of the mouth and the tendency was for them to be confined anteriorly by the bony structure of the palate and face. There was no sign at all of invasion of bone in any case.

The tendency to recur has long been recognized as a property of parotid tumours, although histologically they show none of the cytological features

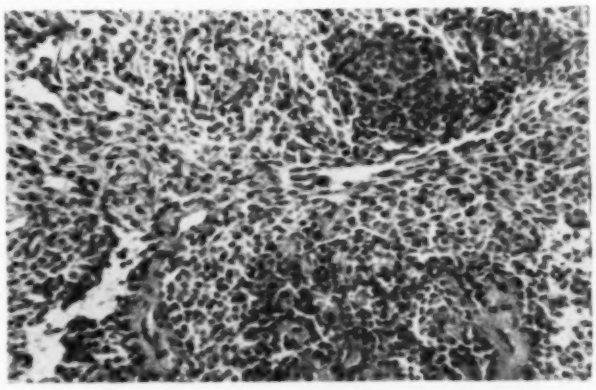


FIG. 611.—*Case* 4. Solid epithelial formation with little acinar pattern.

of malignant growths. This feature is very marked in this small series where one (*Case* 2) recurred within eight months of primary removal, while *Case* 3 showed clinical and histological signs of invasive qualities. The clinical sign of frank malignancy, viz., pain and ulceration, were however absent.

The size of the tumours, particularly the first, would be more remarkable if seen in England, but the Sudanese is still reluctant to come early for treatment and in the first case, the Southern woman, it was perhaps surprising that she came when she did. Though large, this is by no means a record. Street (1913) records parotid tumours of weight up to 115 oz. in Indians, and Balme (1912) one in a Chinese woman which was as large as the patient's head. A very comparable series of four palatal tumours in Chinese patients is recorded by Davis (1935), but none had reached the stage of interfering with deglutition. One significantly had recurred six months after operation. The operations in this series appear to have been enucleations.

TREATMENT

This is entirely operative, though if available one would consider radiotherapy in addition. The operations were extensive, and in *Cases* 1 and 3 formidable. In view of the known tendency to recurrence, excision of the growth with the false capsule is the ideal treatment. McFarland (1936) has demonstrated that recurrence is commonest after curetting the growth, less common after enucleation, and least after dissection. He also makes the observation that the large tumours have least tendency to recur. This is reasonable to expect if the view is accepted that these tumours are multicentric in origin. This ideal of treatment could only be achieved in two cases, *Cases* 2 and 4. In the first

case the size of the tumour alone precluded any treatment more extensive than enucleation, while *Case* 3 showed infiltration and particularly in the region of the base of the epiglottis a fragment of apparently normal tissue showed invasion on section. In all cases apparently normal peripheral tissue was removed, submitted to the pathologist, and in the others there was no sign of spread. Where the

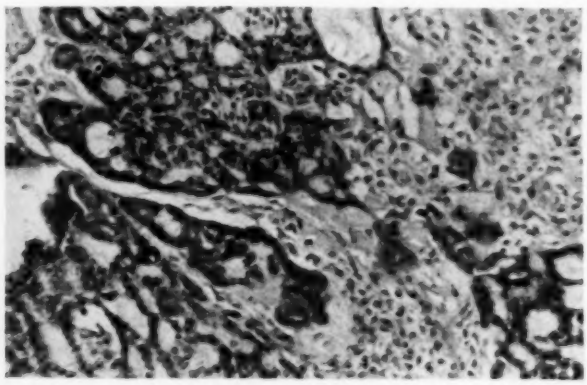


FIG. 612.—*Case* 2. Recurrence, glandular tissue with mucinous matrix.

recurrence had taken place (*Case* 2) the previous operation had been an enucleation which had had perforce to be completed rather hastily in another hospital. In the very large tumours the general prognosis has to be taken into account. Patey (1931), having collected several records from 1904, concludes that the recurrence rate is tending to fall and advises a conservative outlook. It would seem logical where radical operation might endanger life or result in mutilation to advise enucleation and then careful observation. If recurrence occurs radical treatment in the involved area is undertaken, as was in actual fact done in *Case* 2.

FREQUENCY IN RELATION TO OTHER SALIVARY TUMOURS

Willis (1948) has analysed 428 salivary tumours and shown that the approximate percentage of palatal ones is 5 and that of the minor glands about the same. The total numbers of pleomorphic adenomata received in the Stack Laboratories during the three years under review were 37, and, of these, 4 were palatal and 4 were from minor glands of the mouth and tongue. These figures suggest that their relative frequency is much the same in the Sudan as elsewhere in the world.

HISTOLOGY

The term 'pleomorphic adenoma' is used by Willis (1948) and has been adhered to in this text. The chief characteristic of these tumours histologically is their extreme variability in appearance, which has in the past led to speculative theories as to their origin and fanciful nomenclatures, but it is now generally agreed, as suggested by Fry (1928) and Harvey, Dawson, and Innes (1938), that this pleomorphism is merely a result of indifferent nutrition and degeneration and the tumour is essentially an adenoma. The defective nutrition is probably in turn due to their poor blood-supply, which is demonstrated by the fact that enucleation of even the large tumour (*Case* 1) from a highly vascular area of the body was accomplished with very little hæmorrhage. The histological types of salivary tumours have been subdivided into nine classes by Willis (1948), to whose book the reader is referred for details. All the tumours shown here are pleomorphic, though in *Case* 3 the predominating architecture is a cribriform structure. The same specimen demonstrates well invasive qualities without histological malignancy. Patey and McFarland have shown that histological appearance bears little relation to prognosis so far as recurrence is concerned, though the latter does suggest that tumours in which epithelium predominates are more likely to recur. *Fig.* 612 shows that a recurrent growth need not show any histological signs of increased malignancy which Patey (1931) and McFarland (1936) consider the general rule, though Willis (1948) considers that there are exceptions to this.

SUMMARY

Three cases of pleomorphic adenomata arising in the palate and one in the tongue are described.

These growths are slow growing, painless, and capable of growing to a large size. They can recur and infiltrate.

The treatment of choice is adequate surgical removal with a margin of healthy tissue.

Histologically they show the same range of pleomorphism as do the same tumours arising from the major salivary glands.

The relative frequency of these tumours to those of the major salivary glands in the Sudan is about the same as in other countries where records are available.

I am indebted to Dr. Mohamed Ali Zaki, Director of the Sudan Medical Services, for permission to publish these cases; and to Dr. Mansour Ali Haseeb for allowing me access to the records and material available in the Stack Laboratories, Khartoum.

REFERENCES

BALME, H. (1912), *Brit. med. J.*, **1**, 1292.
DAVIS, J. L. (1935), *J. Path. Bact.*, **41**, 289.
FRY, R. M. (1928), *Brit. J. Surg.*, **15**, 291.
HARVEY, W. F., DAWSON, E. K., and INNES, J. R. M. (1938), *Edinb. med. J.*, **45**, 275.
MCFARLAND, J. (1936), *Surg. Gynec. Obstet.*, **63**, 457.
PATEY, D. H. (1931), *Brit. J. Surg.*, **18**, 241.
STEINER, P. E. (1954), *Cancer: Race and Geography*, 312. Baltimore: Williams & Wilkins Co.
STREET, A. (1913), *Brit. med. J.*, **1**, 1047.
WILLIS, R. A. (1948), *Pathology of Tumours*, 324. London: Butterworth.

CARCINOMA OF THE UTERINE TUBE

A REVIEW AND A DESCRIPTION OF A CASE WITH UNUSUAL CLINICAL FEATURES, PRESENTING AS AN ACUTE ABDOMINAL EMERGENCY

By W. F. W. SOUTHWOOD, London

Carcinoma of the uterine tube is an uncommon tumour and the rarest of all primary cancers of the female genitalia (Boyd, 1953). In a survey of 14,182 primary tumours only 3 were found to have arisen from the uterine tube (Harnett, 1952), an incidence of 0·021 per cent. Altogether approximately 500 cases have been described.

HISTORICAL

Renaud (1847) described the gross condition for the first time and Rokitansky (1861) was the first to give an account of the microscopical appearances. Orthmann (1886) reviewed the 13 cases previously described in the literature and excluded them as representing metastatic disease from a primary focus in the uterus or ovary; at the same time he described the first accepted case of primary adenocarcinoma of the uterine tube.

Orthmann's original case was followed by 17 cases collected by Sanger and Barth (1895). Peham (1903) was able to collect 63 cases. Doran (1910) carefully reviewed the 100 cases reported up to that time. Liang (1926) gathered 214 cases, of which 107 were from the German literature; this was increased to 230 cases by Wharton and Krock (1929), who described 14 additional specimens. Robinson (1936), describing 3 cases of his own, reviewed a further 48 cases, bringing the total to 349. Martzloff (1940) reviewed 383 cases in the literature when describing a case of his own. Mullins and Mosteller (1943) described a further case and stated that 427 cases had been reported up to that time. Carpenter and Jameson (1952) described a further 5 cases, bringing the total to 503 cases, and subsequently only about 30 more cases have been found. The literature on this subject comes almost entirely from Germany or America; very few examples have been recorded in this country.

PATHOLOGY

Carcinoma of the uterine tube is frequently associated with chronic salpingitis; this association is so common that some authors (Le Count, 1901; Cruttenden and Taylor, 1950) believe that salpingitis is of aetiological significance. The tumour is bilateral in one-third of the cases and usually involves the ampullary portion of the tube.

Spread.—

1. Direct spread to the muscle coat and serosa and later transperitoneally.
2. Luminal spread to the uterine cavity, cervix, and vagina.
3. Lymphatic spread:—
   (i) To iliac, lumbar, and pre-aortic nodes;
   (ii) Less frequently to the inguinal nodes;
   (iii) Occasionally to the nodes along the utero-sacral ligament.
4. Blood spread, usually to liver and lungs.

HISTOPATHOLOGY

The most widely accepted classification is that of Sanger and Barth (1895):—

1. Papillary Carcinoma.—The tumour is confined to the lumen and the transition between normal and malignant tissue is clearly seen. The tumour is well differentiated and mitoses are infrequent.

2. Papillary-alveolar Carcinoma. — The tumour shows early glandular formation and there is early invasion of the tubal wall. The individual cells are undifferentiated and there are a moderate number of mitoses.

3. Alveolar-medullary Carcinoma. — The tumour shows no papillary projections and the cells are arranged in a medullary or glandular pattern; the cells are poorly differentiated and there is early invasion of lymphatic vessels in the tubal wall.

Orthmann (1886) pointed out that many of these tumours are metastases, usually from the uterus or ovary. To differentiate a primary from a secondary tumour the criteria laid down by Hu, Taylor, and Hertig (1950) must be fulfilled:—

1. The main tumour must lie in the tube.
2. Microscopically the tumour should show a papillary pattern.
3. If the tubal wall is found to be involved to a great extent the transition between benign and malignant tissue should be demonstrable.

CLINICAL FEATURES

Pain and vaginal discharge are the two commonest presenting symptoms. Pain when present usually appears early in the disease (Mitchell and Mohler, 1945); it is usually situated in the lower abdomen and is described as being dull, crampy, or intermittent in character. Lofgren and Dockerty (1946) state that the pain is never acute. The vaginal discharge varies in character from leucorrhœa to a blood-stained discharge, and the latter symptom occurring after the menopause is very suspicious.

The symptom-complex of intermittent colicky pain, associated with a constant, intermittent, or sudden gush of clear yellow or blood-stained fluid per vaginam and subsequent relief of pain, is called 'hydrops tubæ profluens'; it is very suggestive of carcinoma of the uterine tube. It was first described by Roberts (1898a, b) and later by Edelberg (1912).

Other less common presenting symptoms are abdominal swelling, backache, dysuria, and frequency.

Physical signs are few. In an early case it is sometimes possible to feel a mass in the pelvis; later an abdominal mass may be palpable and there may be ascites or evidence of metastases.

DIAGNOSIS

A pre-operative diagnosis of carcinoma of the uterine tube is seldom made, and out of over 500 cases reported a pre-operative diagnosis has been claimed in

less than 10. In cases which present with a blood-stained vaginal discharge and where uterine curettage is negative, carcinoma of the uterine tube should be considered in the differential diagnosis. Hydrops tubæ profluens is a very significant symptom, but unfortunately is not very common.

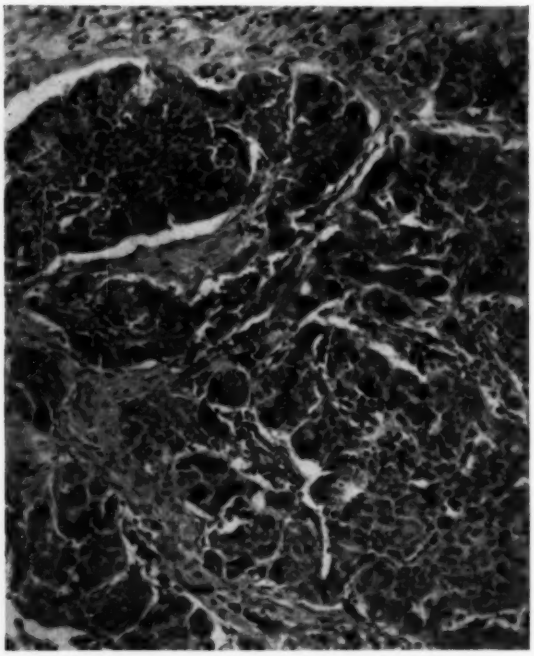


FIG. 613.—Section through the main mass of the tumour, illustrating its anaplastic structure. (× 105.)

Falk (1898) recommended cul-de-sac puncture in order to withdraw the contents of a carcinomatous tube adherent to the pelvic peritoneum; the use of this method enabled him to be the first to establish the diagnosis pre-operatively. More recently salpingography has been suggested as a diagnostic procedure (Martzloff, 1940; Vessell and Schneider, 1947), but this is probably almost as dangerous. The development of the Papanicolaou technique of smear diagnosis (Papanicolaou and Traut, 1943) will probably result in the pre-operative diagnosis being made more frequently in future.

TREATMENT

For many years total hysterectomy, bilateral salpingo-oöphorectomy, and dissection of the pelvic and sometimes the inguinal lymph-nodes was the universally accepted treatment. The results have been poor and Block (1947) recommends that bilateral salpingo-oöphorectomy only should be performed and that radium should subsequently be inserted into the uterine cavity. He reports encouraging results using this technique. The recent development of high-voltage external irradiation may prove of considerable value in the treatment of this tumour.

CASE REPORT

The following case presented with unusual clinical features.

Mrs. H. P., a nulliparous woman aged 52, was admitted to the Royal Masonic Hospital as an emergency in May, 1954, with the provisional diagnosis of acute appendicitis. She had a 12-hours' history of continuous hypogastric pain; there was marked anorexia, but no nausea or vomiting. There were no urinary symptoms and her menopause had occurred two years previously. She had never had any vaginal discharge.

Her tongue was furred; there was marked tenderness and guarding in the right iliac fossa and rebound tenderness was present. On rectal examination there was tenderness on both sides of the pelvis, but no mass could be felt.

The diagnosis of acute appendicitis was made and immediate operation decided upon. In view of the slightly unusual features, the abdomen was explored through a right lower paramedian incision. Free fluid was present in the peritoneal cavity. The appendix was found to be normal, but a large swelling of the right uterine tube was present; the ovaries, left uterine tube, and uterus appeared normal. Right salpingectomy was performed.

Post-operatively the tube was opened and it was found that there was evidence of recent hæmorrhage into the lumen; an irregular mass was seen at the ampullary end of the tube, but the serous surface was not involved. Microscopical examination showed the presence of a poorly differentiated adenocarcinoma of high-grade malignancy (*Fig.* 613).

Her convalescence was uneventful, and in view of the anaplastic nature of the tumour it was thought that early radiotherapy would be of greater benefit than a more extensive operation. She was therefore referred to Dr. Moore Patterson, who irradiated the whole pelvis with a homogeneous dose of 4000 r, using four portals.

The patient, when last seen in January, 1957, was found to be in good health, had no abdominal symptoms, and had gained weight. No evidence of recurrence of the growth was found.

DISCUSSION

Of the case histories reported in the literature 302 were studied and it was found that pain was a presenting symptom in 181 patients. In no case was either guarding or rebound tenderness recorded as having been present, although 1 case which occurred in 1926 and was reported by Edwards and Beebe (1947) presented with similar symptoms and further inquiry (Beebe, personal communication) showed that guarding was present. The recent hæmorrhage from this anaplastic tumour was probably responsible for the physical signs and it is interesting to note that Beebe's case, too, showed evidence of recent hæmorrhage.

The majority of authors comment on the poor prognosis in this disease. Stern and Hanley (1949) in a series of 48 cases found a 5-year survival rate of only 6 per cent. In the series of 12 cases reported by Hu and others (1950) the 5-year survival rate was 40 per cent; 5 of these cases were anaplastic carcinomas, all of which died between 5 and 27 months post-operatively. Although Bancroft-Livingstone (1946) doubts the value of radiotherapy, it seems probable that the recent developments in this science are likely to improve the prognosis in tubal carcinoma.

SUMMARY

1. Approximately 500 cases of carcinoma of the uterine tube have been reported in the literature. These are reviewed.

2. A case is presented with physical signs suggesting a diagnosis of acute appendicitis.

I am grateful to Mr. E. A. Crook for permission to publish this case and for his help in the preparation of this paper.

REFERENCES

BANCROFT-LIVINGSTONE, G. (1946), *J. Obstet. Gynæc. Brit. Emp.*, **53**, 453.
BLOCK, E. (1947), *Acta radiol., Stockh.*, **28**, 49.
BOYD, W. (1953), *Textbook of Pathology*, 6th ed., 656. London.
CARPENTER, R. J., and JAMESON, W. J. (1952), *Amer. J. Surg.*, **83**, 595.
CRUTTENDEN, L. A., and TAYLOR, C. W. (1950), *J. Obstet. Gynæc. Brit. Emp.*, **57**, 937.
DORAN, A. (1910), *Ibid.*, **17**, 1.
EDELBERG (1912), *Gynak. Rdsch.*, **6**, 601.
EDWARDS, E. A., and BEEBE, R. A. (1947), *Amer. J. Obstet. Gynec.*, **53**, 1049.
FALK, E. (1898), *Berl. klin. Wschr.*, **25**, 554 and 576.
HARNETT, W. L. (1952), *Survey of Cancer in London*, 529. London: Brit. Emp. Cancer Campaign.
HU, C. Y., TAYLOR, M. L., and HERTIG, A. T. (1950), *Amer. J. Obstet. Gynec.*, **59**, 58.
LE COUNT, E. R. (1901), *Johns Hopk. Hosp. Bull.*, **12**, 55.
LIANG, Z. (1926), *Virchow's Arch.*, **259**, 577.
LOFGREN, K. A., and DOCKERTY, M. B. (1946), *Surg. Gynec. Obstet.*, **82**, 199.
MARTZLOFF, K. H. (1940), *Amer. J. Obstet. Gynec.*, **40**, 804.
MITCHELL, R. M., and MOHLER, R. W. (1945), *Ibid.*, **50**, 283.
MULLINS, D. F., and MOSTELLER, R. (1943), *Ibid.*, **45**, 1042.
ORTHMANN, E. J. (1886), *Zbl. Ges. Gynäk.*, **15**, 212.
PAPANICOLAOU, G. N., and TRAUT, H. F. (1943), *Diagnosis of Uterine Cancer by the Vaginal Smear*. New York.
PEHAM, H. (1903), *Z. Heilk.*, **24**, 317.
RENAUD, F. (1847), quoted by DORAN A. (1896), *Trans. obstet. Soc. Lond.*, **38**, 322.
ROBERTS, H. (1898a), *Brit. med. J.*, **1**, 1263.
— — (1898b), *Trans. obstet. Soc. Lond.*, **40**, 189.
ROBINSON, M. R. (1936), *Amer. J. Obstet. Gynec.*, **32**, 84.
ROKITANSKY, C. F. (1861), *Lehrbuch der pathologischen Anatomie*, **3**, 444. Vienna.
SANGER, M., and BARTH, J. (1895), "Die Neubildungen der Eileiter" in *Die krankheiten der Eileiter*. Martin, A. Leipzig.
STERN, B. D., and HANLEY, B. J. (1949), *Amer. J. Obstet. Gynec.*, **58**, 517.
VESSELL, M., and SCHNEIDER, H. (1947), *Ibid.*, **54**, 140.
WHARTON, L. R., and KROCK, F. H. (1929), *Arch. Surg., Chicago*, **19**, 848.

SARCOMA ARISING IN A CHRONIC ACTINOMYCOTIC SINUS

BY MARTIN A. GOODWIN
SEDGEFIELD GENERAL HOSPITAL

THERE have been several reports of malignant degeneration taking place in discharging sinuses of long standing. Doran (1948) reports a case arising in a chronic anal fistula and refers to other such cases in the literature. Chronic bone sinuses seldom lead to malignant change at their orifices (McAnally and Dockerty, 1949; Marks and Turner, 1950; Gillis and Lee, 1951). In most cases the new growth is carcinomatous in nature; rarely does one find sarcomatous change. The present case is reported as it appears to be unique and I can find no similar condition in a fairly wide search into the literature. Cope (1950) with his wide experience of actinomycosis has never heard of a similar condition.

CASE REPORT

A female patient, aged 24 years, was admitted to hospital on May 17, 1941, with the diagnosis of acute appendicitis. An operation was performed under spinal anæsthesia through a right paramedian approach, and a localized appendix abscess was found and drained. The appendix was not removed. In the early post-operative days there was slight drainage from the tube.

On June 2 pus discharged from the abdominal wound and there was tenderness in the right subcostal area posteriorly. A subphrenic abscess was diagnosed and a radiograph showed that the right dome of the diaphragm was raised, with some effusion present in the costo-phrenic angle. Granules were seen in the pus coming from the wound and actinomycosis was considered.

A report on the examination of the pus was as follows:—

Gram-positive and -negative bacilli and Gram-positive cocci present in very large numbers. No granules were seen in the pus and no evidence of actinomycosis. Predominant organisms on culture were of the coliform group.

On June 5 aspiration of the subphrenic space by an approach below the right twelfth rib was carried out and pus withdrawn. Following this, incision and drainage was carried out and 10–12 oz. of pus were obtained. A tube drain was left in situ.

The discharge grew less and the patient was allowed to go home on July 5. On Sept. 8 the woman was readmitted with the object of doing an interval appendicectomy, but there was a septic blister at the upper end of the previous abdominal incision and the operation was not done. Further radiographs of the abdomen still showed a raised right dome of the diaphragm with diminished excursion. There was also a discharging sinus in the right subcostal area posteriorly and some of the tissue from the sinus opening was sent for bacteriological examination.

The film showed a few pus cells and necrotic material. No tubercle bacilli or other organisms were seen and culture yielded no growth. She was discharged from hospital on Sept. 23 and referred to her own doctor.

Re-admission to hospital took place on Feb. 9, 1944, because of pain in the right iliac fossa and slight pyrexia. She had been perfectly well since she last left hospital. For a few days prior to admission she had diarrhœa and had vomited twice in the last twenty-four hours. She

looked pale, but had not lost weight. The old subphrenic abscess sinus was still discharging. There was tenderness and rigidity in the right iliac fossa and a mass about 2 in. in diameter could be felt. Her temperature was 101·6° F., pulse 122 per min., and respiration 24 per min. She had a leucocytosis of 13,000 per c.mm. Pus from the sinus was again taken for culture and on this occasion actinomyces were found.

She was reviewed again on June 7, 1944, when the mass was felt to be smaller and she was again discharged.

FIG. 614.—The fungating mass in the right loin, showing the multiple sinuses and areas of necrosis.

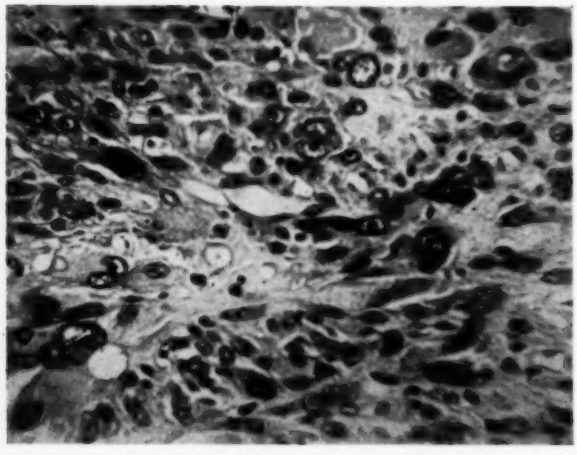


FIG. 615.—A highly cellular anaplastic sarcoma. (×225.)

In November, 1944, and February, 1945, she was an in-patient and was given penicillin therapy.

Admission again took place on Jan. 12, 1948, when the sinus in the right loin had been discharging for two months. Her general condition on this occasion was very poor and she had lost weight. Furthermore, fæcal matter was discharging from the sinus. There was some abdominal distension. The right flank showed multiple sinuses discharging fæces and pus, with discoloration of the surrounding skin. Several indurated masses could be felt in the abdomen and rectal palpation showed a hard mass on the left side. Repeat examination of the discharge from the sinuses failed to reveal actinomycosis.

Laparotomy was decided on and performed on March 1, 1948, under local anæsthesia. Through a left paramedian subumbilical incision the abdominal cavity was opened, and immediately an abscess cavity was discovered. It extended down to the pelvic brim and reached up to the left loin. The walls were firm and almost cartilaginous. A portion of the lining was excised for histology and the abdomen was closed. Blood transfusions were given before and after operation. She was discharged from hospital on June 23 and continued to attend as an out-patient.

Bacteriology of the pus taken at the laparotomy :—

Microscopical examination : Films show numerous pus cells and Gram-positive filamentous organisms resembling a streptothrix. No tubercle bacilli found.

Culture : Anærobic cultures yield a growth of an organism morphologically resembling *Streptothrix actinomyces*.

Pathological report on wall of abscess cavity : Four pieces of pink, firm tissue each 0·75 cm. in diameter and 4 mm. in thickness.

Histology : Section shows an abscess wall consisting of pyogenic exudate and a fibrous wall infiltrated with chronic granulation tissue. The Gram stain of the section shows an area in which a small focus of actinomyces is present, consisting of Gram-positive branching filaments. The bacteriological examination revealed an organism which gave the morphology and cultural characteristics of actinomyces.

The patient attended regularly for a while and then failed to report. The next occasion that she was seen was in June, 1949, when she presented herself with a large fungating mass in the right flank (*Fig.* 614). There was extensive induration around the mass, which was covered with purulent areas and discharging points. Her general condition was poor. The blood-count showed R.B.C. 4,090,000 c.mm., Hb 35 per cent, C.I. 0·4, and a leucocytosis of 12,200 c.mm. She was admitted to hospital on June 12, 1949, and was put onto iron therapy and blood transfusions. A swab taken from the area showed a few pus cells and numerous Gram-negative bacilli ; culture gave a growth of Proteus. Under intravenous pentothal anæsthesia the fungating mass was removed. It was necrotic and foul smelling, with pockets of pus. Bleeding was excessive.

The *pathological report on the specimen* was as follows :—

Specimen received in formalin 7×6×2·5 cm. On section it consists of soft œdematous pink tissue with a fibrous capsule containing blood-vessels. The centre contains a circumscribed red area with pus.

Microscopical examination: Histologically the bulk of the tissue consists of a highly cellular anaplastic sarcoma which is invading infected granulation tissue. In view of the long-standing actinomycotic infection in this case the tumour is most probably a granulation-tissue sarcoma (*Fig.* 615).

Arrangements were made for radiotherapy to the tumour site. It was astonishing to see how soon the tumour began to proliferate after its removal. The first course of X-ray therapy appeared to keep the proliferation in check. On Oct. 14, 1949, severe hæmorrhage occurred from the sinus in the right loin and despite blood transfusions she died on Oct. 19, 1949.

POST-MORTEM EXAMINATION.—

External appearance: A pale, moderately well-nourished subject. There was a large sinus in the right loin which was approximately 6 in. in length. A small sinus was also present on the anterior abdominal wall.

Heart and blood-vessels: The heart was of normal size but the musculature somewhat atonic.

Lungs and air-passages: Both lungs showed some congestion in the lower lobe, but no evidence of infection.

Alimentary passages and peritoneum: Dense adhesions were present in the peritoneal cavity. The stomach was firmly adherent to the liver and great difficulty was encountered in separating the spleen from the liver. In this area a small pocket of pus was present. The sinus of the loin communicated with the cæcum and the posterior abdominal wall behind the cæcum consisted of hard fibrous tissue. The uterus was adherent to the rectum and a pocket of pus was present in this area. The posterior abdominal wall on the right side was thickened and contained pockets of pus over the necks of the ribs and also the lumbar vertebræ. The psoas muscle on the right side consisted of dense, firm fibrous tissue.

Liver and gall-bladder: The liver was slightly larger than normal and fatty in consistency.

Spleen: The spleen was enlarged and showed translucent areas consistent with amyloid disease.

Kidneys: The left kidney was extremely pale but did not show any macroscopic evidence of disease. The right kidney, which was surrounded by dense fibrous tissue, was pale but did not show any evidence of infection.

Skull, meninges, brain, cord, and nerves: Not examined.

MICROSCOPICAL EXAMINATION.—Section of *cæcum* shows ulceration of a portion of the mucosa which consists of granulation tissue with a superimposed pyogenic exudate. The muscle coat and serosa in this area is also infected and contains numerous chronic inflammatory cells. There is no evidence of actinomyces infection.

Section of *psoas muscle* on the right side shows almost complete replacement of the muscle tissue by fibrillary tissue. There is no evidence of infection or new growth.

Section of tissue from the *posterior abdominal wall* shows chronic granulation tissue with a superimposed acute infection.

Section of *liver* shows gross fatty change.

Section of *kidney* does not show any evidence of amyloid disease.

Cultures of the pus from the regions of the *spleen* and *rectum* did not contain any actinomyces.

DISCUSSION

Chronic irritation has long been recognized as a cause of malignancy. It is perhaps not entirely surprising to find reported cases of malignant changes at the cutaneous orifice of chronic sinuses or fistulæ.

Fistulæ-in-ano and osteomyelitic sinuses of long standing are *a priori* conditions where the skin around the external orifice, being constantly subjected to the irritant effects of the discharges, may be expected to show in time carcinomatous degeneration. Despite the frequency of these sinuses, particularly those of osteomyelitis in the past, the number of reported cases of malignant change are few—4000 cases of osteomyelitic sinus at the Mayo Clinic when studied showed carcinomatous changes in only 0·23 per cent (McAnally and Dockerty, 1949). There were no sarcomata. Benedict (1931) found 12 patients developing carcinoma in a review of 2400 cases of osteomyelitis. The case described above is most unusual because as far as I can ascertain no previous case of sarcomatous change in an actinomycotic sinus has ever been reported. Scott (1955) reports an epithelioma of the abdominal wall developing on an actinomycotic sinus. He was of the opinion that the malignant change was not due to the abdominal actinomycosis, but associated it with the repeated exposures of the abdominal wall to X-ray therapy.

There appear to be only two other cases of sarcomatous change in a chronic sinus reported and both these arose in connexion with osteomyelitis (Kirshbaum, 1949; Waugh, 1952).

Why should sarcoma develop when in the majority of these cases epitheliomatous degeneration would be expected? In the case reported by Waugh the histological findings showed that the tumour arose from the connective tissue.

All sinuses and fistulæ are lined with granulation tissue, and over a long period of years it may be permissible to postulate that the cellular element of the granulation tissue proliferates beyond all control with resulting sarcomatous change.

To quote Hadfield (1951): "The essential function of granulation tissue is to replace useless material by living mesenchyme. This is achieved by a process of vigorous vascular and cellular invasion just as aggressive and at least as rapid as the infiltration of normal tissue by a malignant tumour."

Ewing (1942) introduced the entity of 'granulation-tissue sarcoma', but I have failed to find any report of such a case and standard works on pathology do not mention the condition or give it scant attention. Most pathologists I have spoken to consider with great reserve the existence of such a sarcoma. The case reported here has further interest in that the sinus was an actinomycotic one. The dense fibrous tissue reaction so typical of infection with actinomycosis is well known. Cope (1949) in his Bradshaw Lecture suggested "that the stimulator of the mesenchyme cells comes from some degenerative or secretory product of the organism itself . . . it seems reasonable to assume that the extraordinary stimulus of fibrous tissue formation comes from the actinomyces". In the case presented here it may be that the presence of some product of the organism stimulated excessive fibrous tissue reaction which resulted in sarcomatous change.

My thanks are due to Dr. L. Stent of the Pathology Department, Withington Hospital,

Manchester, for the bacteriological and histological reports ; and to Dr. B. E. Tomlinson, of the Department of Clinical Pathology, Newcastle General Hospital, for the photomicrograph.

REFERENCES

BENEDICT, E. B. (1931), *Surg. Gynec. Obstet.*, **53**, 1.
COPE, V. Z. (1949), *Brit. med. J.*, **2**, 1311.
— — (1950), personal communication.
DORAN, F. S. A. (1948), *Brit. J. Surg.*, **36**, 100.
EWING, J. (1942), *Neoplastic Diseases*, 4th ed., 164. Philadelphia : Saunders.
GILLIS, L., and LEE, S. (1951), *J. Bone Jt Surg.*, **33B**, 167.
HADFIELD, G. (1951), *Ann. R. Coll. Surg. Engl.*, **9**, 397.
KIRSHBAUM, J. D. (1949), *J. Bone Jt Surg.*, **31A**, 413.
MCANALLY, A. K., and DOCKERTY, M. B. (1949), *Surg. Gynec. Obstet.*, **88**, 87.
MARKS, K. L., and TURNER, W. L. (1950), *Brit. J. Surg.*, **38**, 206.
SCOTT, L. B. (1955), *Brit. J. Plas. Surg.*, **8**, 158.
WAUGH, W. (1952), *J. Bone Jt Surg.*, **34B**, 642.

BILATERAL WILMS' TUMOUR

BY P. P. RICKHAM, LIVERPOOL

" However true it may be that some diseases baffle the skill of the medical practitioner, resisting all his curative and palliative attempts, yet these disappointments ought never so to influence his mind as to damp his exertions, or restrain his endeavours in acquiring a more accurate knowledge of the malady under which his patient labours, for as diseases become more difficult to remove, so should his researches become the more unwearied and assiduous. . . ."

THUS wrote Dr. Rance of London in 1814 when, eighty-five years before Wilms' classical description, he reported the first case of nephroblastoma. These words are as true to-day as they were 140 years ago,

FIG. 616.—*Case* 1 shortly before his death.

for in spite of great advances in surgery and radiotherapy the prognosis for Wilms' tumours is still poor. There has, however, been some improvement in the general outlook for unilateral Wilms' tumours and recent reports, notably from the Children's Medical Centre in Boston, have been more optimistic (Gross, 1953). On the other hand, the prognosis for bilateral Wilms' tumours appears to be so hopeless that it might well " damp the exertions " of the surgeon who is called upon to deal with such a case. Although this gloomy outlook when considering bilateral Wilms' tumours is undoubtedly justified, this paper is presented in order to try to correct the impression that the condition must, of necessity, invariably be fatal.

CASE REPORTS

Case 1.—Alan B. was admitted to Alder Hey Children's Hospital in February, 1949, when 9 months old. His mother had noticed a lump in his right side three days prior to admission. He had no symptoms referable to the urinary system.

FIG. 617.—*Case* 1. Post-mortem specimen showing the two kidneys and the bladder. The left kidney has been sectioned. The circumscribed tumour and the normal lower pole of the kidney are well shown.

On examination, he was thin and pale ; there was a large, apparently cystic mass in the right loin and another smaller mass was felt in the left loin. Examination of the urine showed scanty leucocytes and a considerable amount of albumin. At cystoscopy, the bladder appeared normal and retrograde pyelography showed marked distortion of the pelves of both kidneys.

A diagnosis of bilateral Wilms' tumour was made. Radiotherapeutical opinion advised against radiotherapy on the grounds that both kidneys would be destroyed by irradiation. The tumours grew very quickly and the child became progressively more emaciated. His appearance was soon pitiful, with enormous tumours protruding from both loins, a grossly distended abdomen, and marked œdema of the legs (*Fig.* 616). In spite of this,

he miraculously lived for a further ten weeks, when he finally died of a terminal bronchopneumonia.

AT AUTOPSY.—Both loins were occupied by huge nephroblastomata. The right tumour was the larger; it consisted of confluent spherical masses of firm white tissue, bulging on section and showing a concentric laminated appearance. In some areas there was evidence of recent hæmorrhage. Only in one small area in the plane of the pelvis could normal renal tissue be found. On the left side, the lower fourth of the mass consisted of normal kidney tissue separated by a clear line of demarcation from the neoplasm which constituted the bulk of the mass (*Fig.* 617).

Histological examination showed that both tumours consisted of loose mesenchymal tissue containing islands of small, round undifferentiated cells with occasional formed tubules and strands of smooth muscle. The lower pole of the left kidney was normal in structure, in which no foci of embryonic tissue could be discovered. A detailed dissection of the renal veins, inferior vena cava, heart, and lungs and serial sections of the para-aortic lymph-nodes revealed no metastases, nor were metastases found in any other part of the body.

Case 2.—Linda S. was first seen by Dr. E. G. G. Roberts at the beginning of May, 1954, with one week's history of vomiting and abdominal distension. Her state of nutrition was fair; she weighed 9280 g.

On examination, large tumours were felt in both loins. The right tumour was the larger of the two and gave the impression of being partly cystic (*Fig.* 618). Urine examination showed the presence of a large amount of albumin and numerous red blood-cells. An intravenous pyelogram showed no excretion of the dye on the left side; on the right side a few of the lower calices secreted satisfactorily. The right kidney appeared to be displaced downwards into the pelvis by a large mass at its upper pole. A diagnosis of bilateral Wilms' tumour was made and the child was transferred to the Royal Liverpool Children's Hospital.

Radiographically the lungs, skull, and long bones revealed no metastases. The hæmoglobin was 95 per cent and the blood-urea 36 mg. per cent.

OPERATION was performed on the day of admission. The tumours were approached through a long transverse infra-umbilical transperitoneal incision stretching from the right postrenal angle to the left loin. A very large, apparently encapsulated tumour arose from the upper pole of the right kidney; it occupied the entire right abdomen from the liver to the pelvic brim. The tumour was supplied by large branches of the renal artery and vein; these were tied and divided. The renal artery was then temporarily clamped with a bulldog clamp and the tumour dissected off the remnant of the right kidney with the diathermy needle. A thin layer of kidney substance was removed with the tumour, leaving only the lower two-fifths of the right kidney. The right adrenal gland was left in situ. The left kidney was replaced by a large tumour and was excised after ligating the renal vessels, leaving the left suprarenal gland in situ. The para-aortic glands and the perirenal fat were removed on both sides. One pint of blood was given during operation.

The child stood the operation fairly well. Post-operatively, she was given a further half-pint of blood and for the next three days was kept on continuous gastric suction and intravenous infusions. For the first twenty-four hours post-operatively she was given 7·5 mg. of cortisone t.d.s.; during the next day 7·5 mg. were given b.d. and a further 7·5 mg. on the third day.

Her systolic blood-pressure rose to 150 mm. of mercury during the first twelve hours after operation, but fell to 135 on the second day and 100 on the third day. The temporary hypertension, coupled with an adequate intravenous fluid intake, produced a marked diuresis. Oral feedings were started on the fourth post-operative day and on the fifth day she was transferred to the Christie Hospital and Holt Radium Institute, Manchester (*Fig.* 619).

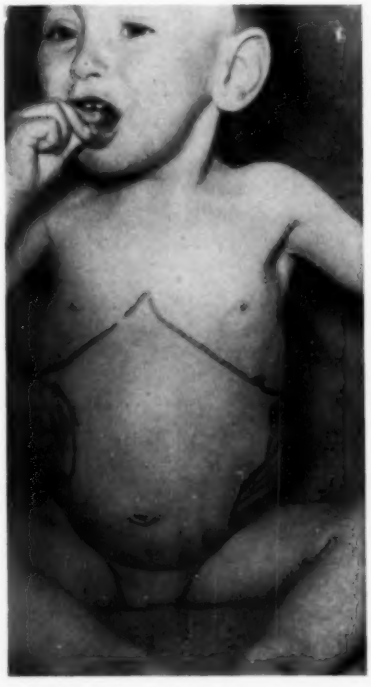


FIG. 618.—*Case* 2 before operation. The tumours are outlined on the skin.

FIG. 619.—*Case* 2 ten days after operation, showing the extent of the incision.

FIG. 620.—*Case* 2 eighteen months after operation.

I am obliged to Dr. Edith Paterson for the following summary of the course of radiotherapy: "She was given radiotherapy to the whole abdomen, the fields being 30 × 22½ parallel opposing. The voltage was 250 kV. and the half-value layer 1·5 mm. of copper. The over-all time was 31 days. The given dose on each field was 1700 r. The tumour dose was 2800 r, but the remains of the right kidney were shielded after a dose of 2000 r had been given in this region."

FIG. 621.—*Case* 2. The excised right nephroblastoma. The tumour is split in the coronal plane.

PROGRESS.—At the conclusion of the course of radiotherapy the child was sent home. She remained thin and delicate and during the following winter had several attacks of upper respiratory infections. Her blood-urea varied between 70 and 80 mg. per cent during the first six months after operation. At first, her weight remained stationary, but a further 6 lb. were gained during the third six-months' period. Repeated radiographic examinations of chest and bones have not shown any metastases; her white blood-count and E.S.R. are normal. Intravenous pyelograms demonstrate that the remaining part of the right kidney has greatly hypertrophied and secretes the dye well. Kidney function as measured by the urea clearance test 14 months after operation is within normal limits. She is now quite a bonny child, growing and gaining weight at the normal rate (*Fig.* 620).

The right tumour weighed 680 g. and the left 450 g.; together they equalled about one-eighth of the total body-weight of the child.

The right tumour was 14 × 9 × 9 cm. in size; the cut surface was greyish-white and bulged on section and had a uniform whorled appearance; a thin layer of renal tissue was attached to its lower aspect (*Fig.* 621).

The left tumour appeared well encapsulated and measured 6 × 6 × 8 cm. It bulged on section and was in appearance similar to the one on the other side. Below the tumour there was a small cyst in the lower pole of the kidney. The renal pelvis was grossly dilated and occupied by a papilliferous mass (*Fig.* 622). The histological picture of both tumours was the same—that of a classical embryoma of the kidney.

DISCUSSION

Incidence.—Wilms' tumour is not a common neoplasm and bilateral tumours appear to be rare. In a recent survey of the literature, Scott (1955) collected details of 906 cases of Wilms' tumour, 33 of them bilateral. In the largest series published in the literature (Gross and Neuhauser, 1950) there were only 4 bilateral cases amongst a total of 96. In over 80 cases of Wilms' tumour seen at the Hospital for Sick Children, Great Ormond Street, during the last thirty years there was not one bilateral one (White, 1955). It is quite possible that a number of bilateral Wilms' tumours have never been reported because of the hopelessness of the condition. Only a comprehensive tumour census carried out over many years will settle the question of the incidence of bilateral nephroblastomata.

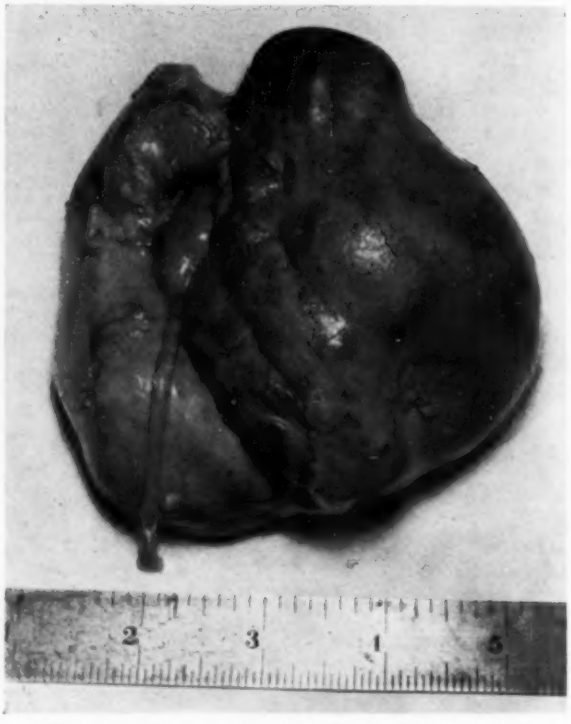


FIG. 622.—*Case* 2. The excised left kidney, which is completely replaced by tumour tissue. The pelvis of the kidney was distended with papilliferous tumour growth.

I am indebted to Dr. J. Fulton of the Liverpool Radium Institute for providing me with details of Wilms' tumours recorded in the tumour register of the region of the Liverpool Hospital Board since the beginning of 1949. The population of this region is slightly over 2,000,000 and 25 cases of Wilms' tumours are recorded, 2 of them (the cases reported in this paper) being bilateral. The series of cases is too small for any conclusion to be drawn from it.

Aetiology.—The question whether bilateral Wilms' tumours are separate primary growths or whether one kidney is primarily affected and the other involved by metastatic spread has often been discussed and has recently been reviewed by Scott (1955). This writer is of the opinion that while a few cases are bilateral primary growths, the majority of the reported cases represent a primary in one kidney with metastatic spread to the other kidney. In support of this view Scott (1955) stresses that the majority of bilateral cases were reported before 1900 when treatment of bilateral tumours was in its infancy. It appears unwise to argue from the figures

published in the literature, especially when discussing such an uncommon and fatal disease, as undoubtedly many cases seen by practitioners are never reported at all. As far as our two cases are concerned, there can be little doubt that they were both examples of separate primary growths in both kidneys. A detailed post-mortem examination in the first case, and careful search during operation of the second patient, revealed no metastatic spread across the midline of the body. Dr. Martin Bodian and Dr. L. L. R. White kindly examined sections from the tumours in both cases and came to the conclusion that the evidence pointed towards separate primary growths, as both tumours consisted mainly of clumps of primitive blastema with several abnormal collecting tubules within the blastema, evidence of initiation of abnormal growth in situ.

Treatment and Mortality.—The treatment of Wilms' tumours by immediate surgery, coupled with radiotherapy starting shortly after operation, first practised in the Boston Children's Hospital, has resulted in a considerable improvement in the mortality rate (Gross, 1953). The over-all mortality rate for unilateral cases is, however, still very high. Only one long-term survival of a case of bilateral Wilms' tumour is reported in the literature. This patient was treated by Dr. Ladd over fifteen years ago by performing a right nephrectomy with pre- and post-operative radiotherapy followed by intensive radiotherapy to the opposite kidney (Gross, 1953). Rusche (1951) reported a case of bilateral Wilms' tumour by nephrectomy combined with radiotherapy to the opposite kidney, who was still alive six months after operation, but this child died within the year (Rusche, 1955). Dr. Ovar Swenson has kindly furnished me with particulars of an unpublished case of bilateral Wilms' tumour; this child was seen with a large mass in the left flank and a nephrectomy for Wilms' tumour was performed. Several months later a pyelogram revealed the presence of a Wilms' tumour on the right side. At operation, as much tumour as possible was removed and post-operatively, radiation therapy was given. It was almost a year before evidence of pulmonary metastasis was found; in spite of radiation to the chest, the child died nineteen months after he was originally seen.

The period of survival in our case is, as yet, too short to be certain of cure, but as Gross (1953) has stated, cases of Wilms' tumour which survive for more than a year without metastases have a good chance of ultimate survival. This is the first case treated by nephrectomy on one side and excision of the tumour on the other side. In retrospect, the first case reported in this paper might have done equally well; the distribution of the tumours and the total absence of metastases would have made excision quite feasible.

Excision of such large tumours leaving only a fraction of one kidney behind is, of course, a very severe operation, but with the aid of post-operative cortisone, such extensive and lengthy operations are well tolerated by small children. It is therefore suggested that in bilateral Wilms' tumour it is worth while attempting operation, as in at least a proportion of cases total ablation of all neoplastic tissue can be accomplished.

SUMMARY

Two cases of bilateral Wilms' tumour are described. In one of them, nephrectomy coupled with excision of the tumour on the other side was performed, followed by radiotherapy. This child is alive and well and without any evidence of metastases thirty-four months after operation. The incidence, aetiology, treatment, and mortality rate of bilateral Wilms' tumour is discussed. It is believed that in a proportion of cases the treatment outlined in this paper might change the impression that the prognosis is invariably fatal.

I should like to thank Miss I. Forshall for permission to publish details of *Case* 1 and for her help and advice in the treatment of *Case* 2. My thanks are also due to Dr. E. G. Hall for the pathological reports on *Case* 1 and Dr. R. E. Rewell for the reports on *Case* 2. The operations would not have been possible without Dr. G. J. Rees's anæsthetic skill and his valuable advice on the post-operative management.

REFERENCES

GROSS, R. E. (1953), *The Surgery of Infancy and Childhood*. Philadelphia: W. B. Saunders Co.
— — and NEUHAUSER, E. B. D. (1950), *Pediatrics*, **6**, 843.
RANCE, T. F. (1814), *Med. phys. J.*, **32**, 19.
RUSCHE, C. (1955), personal communication.
RUSCHE, T. F. (1951), *J. Urol.*, **65**, 950.
SCOTT, L. S. (1955), *Brit. J. Surg.*, **42**, 513.
WHITE, L. L. R. (1955), personal communication.

HÆMANGIOMATA IN SKELETAL MUSCLE

By JOHN E. S. SCOTT

FROM THE MIDDLESEX HOSPITAL, LONDON, W.1

HÆMANGIOMATA of skeletal muscle are uncommon, but they produce such characteristic symptoms and signs that their possibility has only to be remembered for their diagnosis to be made. It is because they are rare and their clinical features not known that they are seldom recognized until they are seen by the histologist. It is the purpose of this paper to describe two examples of this tumour, to consider the relevant literature, and to demonstrate the clear clinical picture by which a diagnosis can be achieved.

CASE REPORTS

Case 1.—

HISTORY.—A 21-year-old man (Middlesex Hospital Reg. No. A.10398) presented himself in the out-patient department on April 22, 1954, complaining of a swelling in the right side of the neck which had been present for three months. In the week before he reported the swelling had increased in size but there had been no pain.

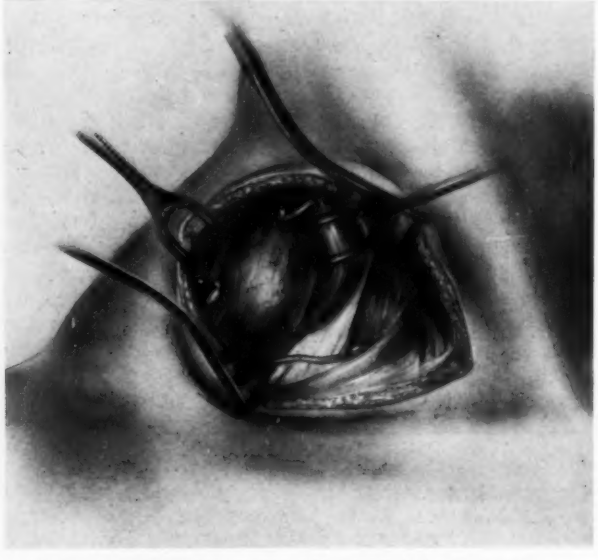


FIG. 623.—Drawing to show the anatomical arrangements and surgical approach in *Case* 1.

Examination showed a smooth, rounded swelling of rubber-like consistency, approximately 1½ in. (3·8 cm.) in diameter, lying deeply in the right posterior triangle of the neck. The swelling seemed to be a lipoma. As it was causing no inconvenience, and the patient was anxious to defer treatment, nothing further was done.

On March 11, 1955, the patient again appeared in the out-patient department complaining that the swelling had increased to such an extent that he was now finding it difficult to do up his collar. He was now ready to have treatment, and his admission to hospital was arranged.

A general physical examination showed no abnormality in the cardiorespiratory system or within the abdomen. A neurological examination with special reference to the right upper limb was also normal. On local examination it was clear that the swelling had increased in size and was now approximately 3 in. (7·6 cm.) in diameter. Otherwise it still bore the same physical characteristics as before; it was smooth, rounded, and not fluctuant; it had a well-defined edge and was mobile in a horizontal direction but not vertically. The overlying skin was not attached to it and was normal. The swelling appeared to be fixed to the deep structures of this part of the neck, but it was difficult to decide whence it arose. There was neither pulsation nor audible bruit. It could not be compressed and was not tender. The teeth, tonsils, and pharynx were all normal and there were no other swellings to be felt in the neck. No enlarged lymphatic glands were found in the axillæ or groins.

A radiograph of the chest was normal, and the hæmoglobin 106 per cent. The W.R. was negative. No radiographs of the neck itself were taken.

No definite pre-operative diagnosis was made but the possibilities seemed to lie between a lipoma, a sarcoma, a neurofibroma, and enlarged lymphatic glands.

AT OPERATION (April 14, 1955).—An incision was made in the line of the skin creases overlying the swelling and deepened through the platysma and the first layer of deep fascia to expose its surface.

FIG. 624.—Macroscopical appearance of specimen from *Case* 1.

Dissection proceeded in front of and behind the mass through the investing layer of deep fascia, and it was at this point that profuse hæmorrhage from its surface commenced and proved difficult to control. The upper part of the brachial plexus was seen lying anterior and medial to the site of dissection and the plane of dissection in front of the tumour appeared to be going deep to the scalenus medius muscle, the outer border of which had to be retracted forwards. The forefinger and thumb were insinuated in front of and behind the swelling and the transverse processes of the cervical vertebræ were palpated behind it. It became clear at this point that the swelling lay in the posterior scalene muscle, which could be felt to contract with each inspiratory movement. *Fig.* 623 illustrates these operative findings. Further dissection towards the lower pole of the tumour revealed a large artery entering its substance and apparently arising from the transverse cervical. This artery was ligated and divided, resulting in a considerable decrease in hæmorrhage from the tumour. It was now possible to identify the tendinous attachments of the muscle to the transverse processes of the cervical vertebræ and these were divided.

The muscle was then traced down behind the clavicle to its insertion into the second rib. This attachment had to be divided blindly, after which the muscle containing the tumour was removed. Hæmostasis was secured and the wound closed in layers with insertion of a small rubber drain.

Healing was uneventful, and the only post-operative disability was anæsthesia of the skin over the front of the clavicle.

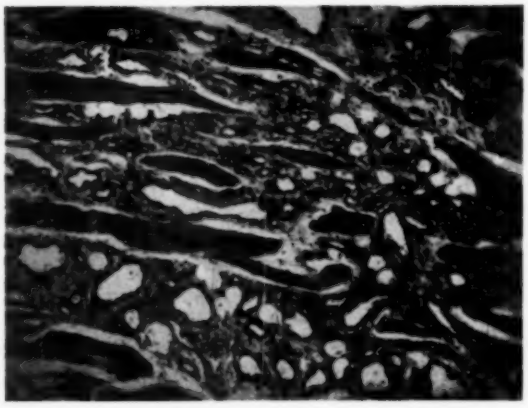


FIG. 625.—Microphotograph of tumour from *Case* 1, showing an area of capillary type of hæmangioma infiltrating between the muscle-fibres.

The patient was last seen in August, 1955, when the wound was soundly healed and there was no discomfort or disability apart from the area of cutaneous anæsthesia.

PATHOLOGY.—

Naked-eye Appearances.—There were normal muscle-fibres separated by firm white tumour tissue with more vascular areas and some large blood-vessels visible on the cut surface (*Fig.* 624).

Microscopical Appearances.—On section there was separation of the muscle-fibres by hæmangiomatous tissue which showed marked variation in different areas. The bulk of the tumour was composed of a capillary type of hæmangioma (*Fig.* 625), but there were in addition more cavernous areas containing large vascular channels (*Fig.* 626), while the more solid parts were composed of sclerosed hæmangiomatous tissue (*Fig.* 627).

Case 2.—

CASE HISTORY.—A man aged 52 years (Middlesex Hospital Reg. No. H.86673) presented himself on May 17, 1955. He stated that he had been born with a swelling in the front of his neck which had been in the midline. At the age of 4½ years this swelling had been excised. Sixteen years later a second swelling appeared in the midline of the submental region. It varied in size, becoming more prominent at night, but would disappear completely from time to time. In the past year the swelling had appeared more frequently, and for two months it had been constantly present. There was an occasional tight feeling in the upper part of the neck. At no time had the variation in size borne any relationship to meals. There were no other relevant features in the history.

No abnormalities were discovered on general physical examination. Local examination of the neck revealed a transverse scar at the level of the upper border of the thyroid cartilage extending almost from the anterior border of one sternomastoid muscle to the anterior border of the other. Above this, lying over the hyoid bone in the midline and extending to the left submandibular region was a bilobed, hard, smooth swelling which was unattached to the overlying skin and was mobile over the deep structures. The swelling was not tender and could be palpated bidigitally with one finger in the mouth; it was obvious that it was not part of the submandibular salivary gland. It appeared solid and the skin overlying it was normal. There were no other swellings in the neck and the regional lymphatic glands were not enlarged. It did not move when the tongue was protruded.

A radiograph revealed a minute circular opacity lying between the hyoid bone and the horizontal ramus of the mandible, which, in retrospect, was probably a phlebolith lying within the tumour. A radiograph of the chest

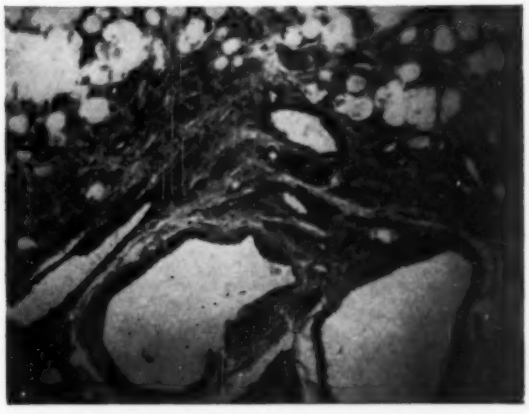


FIG. 626.—Microphotograph of tumour from *Case* 1, showing the more cavernous areas of hæmangioma tissue.

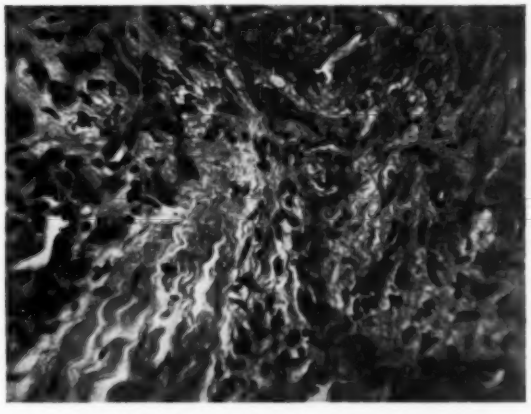


FIG. 627.—Microphotograph of tumour from *Case* 1, showing an area of sclerosing hæmangiomatous tissue.

showed some apical pleural thickening, but the lung fields were clear.

It seemed that the swelling removed in childhood was probably a thyroglossal cyst, and that the one which the patient presented on this occasion might be ectopic thyroid tissue. The only alternative diagnosis which was seriously considered was a mass of enlarged lymphatic glands.

AT OPERATION.—On June 13 the swelling was excised by Mr. D. H. Patey, under whose care the patient had been admitted. An incision was made in the line of the old scar and the upper skin-flap raised to the horizontal ramus of the mandible to expose the tumour. It became apparent that it was situated within the mylohyoid, and was excised with a surrounding margin of normal muscle. During the process of dissection, the anterior end of the left submandibular salivary gland was seen, but it was not involved by the tumour. The incision was closed and apart from a small hæmatoma, proceeded to heal satisfactorily.

The patient was last seen one month after the operation when, apart from some thickening in the region of the

scar, there was nothing abnormal to find on examination and there were no symptoms.

PATHOLOGY.—

Naked-eye Appearances.—The specimen was composed of muscle and firm white tissue measuring 2 × 1 in. (2·6 × 5·2 cm.). On cut section there was firm white tumour tissue interspersed by muscle-fibres.

Microscopical Appearances.—The section showed muscle-fibres between which there was fibrous tissue containing vascular spaces lined by endothelium (*Fig.* 628). Other areas showed extensive sclerosis with virtual obliteration of the hamartomatous capillaries (*Fig.* 629).

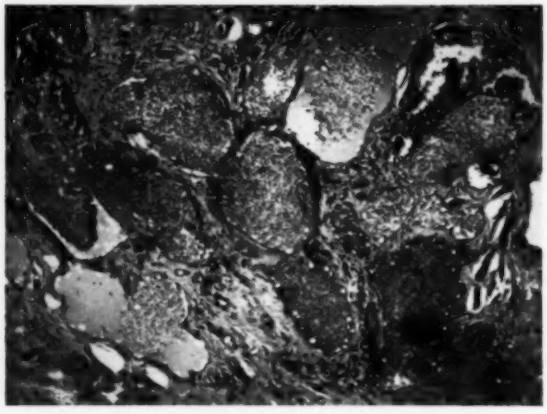


FIG. 628.—Microphotograph of tumour from *Case* 2, showing the endothelial lined vascular spaces lying between muscle-fibres.

FIG. 629.—Microphotograph of tumour from *Case* 2, showing the obliterative sclerosing process in the hæmangioma.

DISCUSSION

Age, Sex, and Site.—Approximately 93 per cent of these tumours occur in persons between birth and 30 years, lending support to the theory of their congenital origin. Tumours occurring in those over the age of 30 have usually been present for many years. The sex incidence is almost equal.

Table I gives the frequency with which hæmangiomata occur in each particular muscle or muscle group. It will be seen that the commonest site is in the lower limb, most often in the quadriceps.

Previously Reported Cases.—The first hæmangioma arising in skeletal muscle was reported by Liston in 1843. It was described as an erectile tumour of the popliteal space, which was found to be an hæmangioma arising in the semimembranosus muscle.

Davis (1908) produced one of the first reviews. He described 1 case which he had treated personally and 5 others which had been treated in Professor Halsted's clinic. To these he added 147 cases collected from the literature. He excluded hæmangiomata which had invaded muscle secondarily from other structures and also those arising in the lip or tongue.

Davis and Kitlowski (1930) published a further review in which they described 11 personally treated cases and summarized a further 48 from the literature, thus bringing the total number of reported cases to 212. There is, however, an isolated case report by Gibb (1913) which is not included in this review.

A very complete study of the subject was published by Jenkins and Delaney (1932), who re-examined the cases collected by Davis and

Table I.—FREQUENCY WITH WHICH HÆMANGIOMATA APPEAR IN DIFFERENT MUSCLES OR MUSCLE GROUPS, EXPRESSED AS A PERCENTAGE OF 393 CASES COLLECTED BY THE AUTHOR

MUSCLE OR MUSCLE GROUP	FREQUENCY	MUSCLE OR MUSCLE GROUP	FREQUENCY	MUSCLE OR MUSCLE GROUP	FREQUENCY
Lower Limb.—		**Upper Limb.—**		**Head and Neck.—**	
Quadriceps	18·9	Forearm flexors	10·3	Masseter	4·9
Calf	13·2	Triceps	4·6	Trapezius	3·2
Hamstrings	4·9	Biceps and Brachialis	2·9	Orbital muscles	1·6
Glutei	2·2	Pectoralis maj.	1·9	Sternomastoid	1·4
Sole of foot	1·6	Thenar muscles	1·9	Temporalis	1·1
Peronei	0·8	Deltoid	1·4	Mylohyoid	0·5
Tibialis anterior	0·8	Palm of hand	1·4	Splenius capitis	0·5
Sartorius	0·8	Ext. carpi uln.	0·5	Scalenus posterior	0·3
Psoas	0·5	Ext. poll. long.	0·3		
Ext. dig. brev.	0·5	Ext. carpi rad.	0·3	*Total*	13·5
Ext. hall. brev.	0·3	Teres maj.	0·3		
Thigh adductors	0·3	Infraspinatus	0·3	**Trunk.—**	
				Abdominal wall	4·3
				Spinal	2·9
				Lat. dorsi	2·9
				Serratus ant.	1·4
				Intercostals	1·4
				Rhomboids	0·8
Total	44·8	*Total*	26·1	*Total*	13·7

Kitlowski and excluded 18 of them. They added 62 cases from the literature and described 1 personal case.

Shallow, Eger, and Wagner (1944) collected a total of 335 cases. They excluded a further 3 cases from those published by Davis and Kitlowski (1930), and described 2 cases treated personally, adding to their series 80 cases collected from the literature. It would appear, however, that 3 of these cases have not been presented with adequate pathological detail and I have deleted them. Also deleted are the cases reported by Fulton and Sosman (1942), because no excision or biopsy was done and the diagnosis was based only on radiological findings. The first three of their cases seem to have suffered from a diffuse angiomatous condition of the upper limb resembling congenital arteriovenous fistula. The fourth case had a diffuse angioma of the sole of the foot which was explored, but the biopsy taken was apparently unsatisfactory. Also excluded are the first 3 of a series of 4 cases described by Pomeranz and Tunick (1941), as again no pathological findings were presented. There are isolated case reports not included in the review of Shallow and others (1944) which warrant mention. Three such cases have been discovered by the author and are included at the beginning of *Table II*.

Bonvallet (1950) reviewed the subject again, adding to the total number of case reports a further 22 which he discovered in the literature, and described 1 case treated personally in which an hæmangioma in the right supinator muscle was removed.

Jones (1953) described 4 cases and reported 15 other cases which had appeared in the literature. One of these, however, that reported by Forconi and Ficai (1948), also appears in the list published by Bonvallet and is therefore excluded from the total.

Since the publication of Jones's article, further case reports have appeared of which the author has studied 5. Sixteen other cases which are not included in the reviews of Bonvallet or Jones have also been discovered and are included in *Table II*, where they are summarized. There are references to another three articles in journals not available to the author. Excluding these articles, the total number of cases proved by histological examination which have been described to date is approximately 393. It will be noted that in one case, that described by Massera (1949), the tumour was actually in the tendo Achillis, not in muscle. As in this case the tumour caused a spontaneous rupture of the tendon it is included because of its unusual mode of presentation. No previous record has been traced in which an hæmangioma arising in the scalenus posterior muscle has been described.

Aetiology.—Many theories have been advanced to explain the histogenesis of these tumours, but it seems likely that they are congenital in origin and are in fact tumour malformations or hamartomata. They would seem to arise in abnormal embryonic sequestrations which retain their embryonic characteristics and extend by establishing a blood-flow in fresh parts of pre-existing malformation. Spread may also be due to metaplastic conversion of proliferating mesenchymal cells which are undergoing predominantly vascular differentiation (Willis, 1953).

Suggestions have also been made that trauma plays an important part in their development (Mailer, 1935). Minor traumata to muscle may lead to the formation of small areas of granulation tissue within the muscle and further repeated minor trauma caused by muscle contraction may stimulate this vascular granulation tissue to proliferate and infiltrate surrounding normal muscle. In approximately 17 per cent of cases there is a history of trauma to the site of the tumour.

Pathology.—

Frequency.—Watson and McCarthy (1940) in a study of 1308 assorted hæmangiomata found that only 0·8 per cent occurred in skeletal muscle.

Pathological Characteristics.—Attempts have been made in the past to subdivide the hæmangiomata into various different groups, such as the capillary, cavernous, circumscribed, diffuse, etc. As their origin seems to be fairly certain, and as their structure varies in different parts, there seems to be little point in maintaining this classification. There is one variety, however, which should be differentiated—the sclerosing hæmangioma. Here sclerosis alters the clinical and microscopical appearances and fibrosis spreads through the tumour, obliterating the vascular channels. These areas will appear less cellular than other parts of the tumour.

The pathological appearances are very constant. Macroscopically, normal muscle-fibres are separated and infiltrated by firm yellowish-white tumour tissue and vascular spaces varying in size appear here and there. Microscopically, proliferating endothelial cells may be seen growing between and separating the striated muscle-fibres. In places these endothelial cells form small vascular channels, while in other places well-formed capillaries and small veins are present. Towards the centre of the tumour the muscle-fibres undergo degeneration, losing their striations and becoming progressively less well-defined until they disintegrate and disappear completely.

Hæmangiomata in muscle are not malignant in the sense that they metastasize. Willis (1953) suggests that cases reported in which true hæmangiomata have apparently metastasized are in actual fact highly vascular connective-tissue sarcomata. Stout (1943) describes 2 cases of metastasizing hæmangiomatous tumours arising in muscle. These tumours fall into a different category, being hæmangioendotheliomata which, it is well recognized, may give rise to metastases and cause death. They occur most commonly in bone.

Although muscle hæmangiomata do not metastasize, they will, if left untreated, infiltrate local tissues to such an extent that any form of local surgical removal is impracticable, and it may become necessary to amputate. Incomplete removal will inevitably be followed by recurrence.

Diagnosis.—Only 8 per cent of those tumours in the literature have been diagnosed pre-operatively, and the 2 cases recorded in this paper are good examples of diagnostic failure. Practically every known pathological swelling has been diagnosed in error. The commonest examples are lipoma, sarcoma, lymphatic glands, muscle hernia, fibroma, and dermoid cyst.

Symptoms and Signs.—The commonest presenting symptom is a swelling which may have been present from one to ten years, or occasionally much

Table II.—SUMMARY OF CASES COLLECTED BY THE AUTHOR WHICH HAVE NOT BEEN INCLUDED IN PREVIOUS REVIEWS

AUTHOR	HISTORY	TREATMENT	SITE	PATHOLOGY
Gibb (1913)		Excision	Biceps brachii	Hæmangioma
Calisti (1943)	Male, 42 yr. Painful tumour along left costal margin for 2 yr.	Excision	Ext. oblique	Hæmangioma
Light (1943)	Male, 16 yr. Pain outer surface right knee for 2 yr., becoming worse. Very tender area present. No swelling	Tender area explored and tumour found in lat. head gastrocnemius	Lat. head gastrocnemius	Hæmangioma
Weaver and Rumold (1943)	Female, 20 yr. Swelling over right great trochanter at 13 yr. Excised when 21 yr. old, but recurred	Excision of most of buttock muscles	Glutei	Hæmangioma
Lazar (1947)	Female, 62 yr. Ill-defined mass front of chest for 5 yr.	Excision	Pectoralis major	Hæmangioma
Massera (1947)	Male, 19 yr. Pain medial surface right thigh for 3 yr. Small swelling present. Radiograph showed opacity	Excision	Adductor longus	Hæmangioma containing bone
Case 34232 (1948)	Male, 15 yr. Pain left calf for 5 yr. Mass present for 3 yr.	Excision	Gastrocnemius	Hæmangioma
Carbonell Antoli and Gomez Sanchez (1949)	Male, 20 yr. Pain in left foot and calf for 10 yr. Separate swelling at each side	Excision of both swellings	Lat. head gastrocnemius	Hæmangioma
Carbonell Antoli and Gomez Sanchez (1949)	Female, 10 yr. Swelling upper third neck for 7 yr. Recently painful	Excision	Sternomastoid	Hæmangioma
Massera (1949)	Male, 53 yr. Sudden pain in region of right heel followed by loss of active plantar flexion	Biopsy of tumour and repair ruptured tendo Achillis	Tendo Achillis	Hæmangioma
Perusi (1951)	Male, 15 yr. Pain in region of left hip for 4 yr. No swelling	Site of pain explored and tumour found in vast. lat. Excised	Vastus lateralis	Hæmangioma
Perusi (1951)	Male, 19 yr. Pain in left thigh for 5 yr. Very tender area at site of pain just above knee	Area of tenderness explored. Tumour found in vast. med. Excised	Vastus medialis	Hæmangioma
Perusi (1951)	Female, 28 yr. Pain inner side right thigh for 4 yr. No swelling	Site of pain explored and tumour found in vast. med. Excised	Vastus medialis	Hæmangioma
Perusi (1951)	Male, 14 yr. Swelling inner side left thigh for 7 yr. Recent pain	Excision	Vastus medialis	Hæmangioma
Pupilli (1951)	Female, 19 yr. Small swelling lat. side left forearm 9 yr. previously. Swelling spread to involve forearm and hand	Amputation	Muscles of forearm	Hæmangioma
Russolillo (1951)	Female, 19 yr. Swelling posterior part left thigh below gluteal fold for some years	Excision	Biceps fem., semitend., glut. max.	Hæmangioma
Russolillo (1951)	Male, 28 yr. Swelling anterior surface right forearm some years	Excision	Palmaris longus	Hæmangioma
Russolillo (1951)	Female, 17 yr. Swelling anterolateral surface left leg for some years	Excision	Peronei	Hæmangioma
Geremia and Fanzago (1952)	Male, 20 yr. Sudden pain and swelling upper two-thirds front of left thigh	Exploration. Sartorius found to be ruptured. Tumour at point of rupture	Sartorius	Hæmangioma
Scheuer (1952)	Child, 6 yr. Swelling of calf when 6 yr. old. Pain and limp present. Dorsiflexion of foot limited	Excision of tumour	Calf muscles	Hæmangioma
Haardt (1953)	Male, 17 yr. Swelling on cheek. Slow increase in size, becoming painful	Excision	Masseter	Hæmangioma
Pelizzolo (1953)	Male, 5 yr. Globular swelling anterior surface upper part left chest	Excision	Pectoralis major	Hæmangioma
Uberti (1953)	Female, 39 yr. Swelling in left calf for 5 yr. Gradual increase in size. No pain or loss of function	Excision	Soleus	Hæmangioma
Willis (1953)	Male. Swelling in rectus femoris at birth	Excision	Rectus femoris	Hæmangioma
Willis (1953)	Female, 21 yr. Ill-defined mass on front of chest for 5 yr.	Excision	Pectoralis major	Hæmangioma

longer. The swelling varies considerably in size, but is usually about 3 in. (7·6 cm.) long. It is rubber-like in consistency, with a smooth surface and a well-defined edge, and may be moved across the line of the muscle from which it arises but not along its length. In most cases it is not compressible and does not have pulsation or bruit, though occasional patients have been reported, particularly in those with tumours in the lower limb, in whom the swelling may become smaller if the limb is elevated, and larger if a venous tourniquet is applied to the limb proximally. The skin over the tumour is usually normal, though occasionally it may be a reddish-blue colour and dilated veins may be seen in the immediate neighbourhood. There is not often tenderness, though this may be present if the tumour is painful. Contraction of the muscle in which the tumour is situated usually renders it more prominent.

The next most frequent symptom is pain, which is present in 58 per cent of cases. The pain is usually over the site of the tumour, but may be referred along a peripheral nerve as a shooting pain. It is thought to be due to compression because these tumours do not actually infiltrate nerves and may be separated from them at operation. In some cases pain may be the only presenting symptom and may become very severe and crippling, and on examination no tumour is found—only an exquisitely tender point. Exploration of the tender point in these cases has revealed an hæmangioma lying deep in the belly of a muscle.

Loss of function and deformity are also common, and occur most frequently as a result of an hæmangioma in the calf muscles. Here, there is loss of active and passive dorsiflexion of the foot. Deformity in the form of a flexion contracture may also occur with tumours situated in the flexors of the forearm. These deformities may be corrected simply by removal of the tumour provided that this is done soon enough.

Radiological studies provide important evidence in diagnosis, as phleboliths may be seen within the soft-tissue swelling. Had this fact been realized at the time that *Case* 2 was under consideration, the correct diagnosis might have been made. Wakeley (1921) appears to have been the first to recognize the presence of phleboliths within these tumours. A diagnosis has been made in some cases by injecting radio-opaque substances into the tumour and outlining dilated vessels in the neighbourhood.

Treatment.—The ideal method of treatment is by complete excision of the tumour with a surrounding margin of normal muscle. Incomplete removal will inevitably result in later recurrence. Many large vessels may be encountered in the neighbourhood of the tumour which may cause troublesome hæmorrhage during the operation. Also, the tumour itself, being vascular, may bleed excessively! Should the tumour be situated in a limb, an Esmarch's bandage or inflatable cuff will control hæmorrhage. In cases where the tumour has spread to such an extent that local removal is impossible, amputation may have to be considered.

Other methods of treatment, such as the injection of sclerosing fluids and irradiation, have been tried and may cause temporary regression of the tumour and loss of pain, but their effect is only temporary.

SUMMARY

Two cases of hæmangiomata arising in skeletal muscle are described.

The past literature is reviewed, and the aetiology, pathology, diagnosis, and treatment of these tumours are discussed.

Acknowledgements.—The author would like to thank Mr. D. H. Patey and Mr. J. H. L. Ferguson, of the Middlesex Hospital, for their permission to publish the cases which were admitted under their care; Mr. R. S. Handley for help in the preparation of this paper; Dr. Drew Thompson for his pathological reports and microphotographs; Mr. Turney for the photograph of the specimen; Miss Hewland for the drawing; and various friends for their help with translations.

REFERENCES

BONVALLET, J. M. (1950), *Pr. méd.*, **58**, 535.
CALISTI, D. (1943), *Prensa med. argent.*, **30**, 895.
CARBONELL ANTOLI, D. C., and GOMEZ SANCHEZ, J. (1949), *Medicina, Madr.*, **17**, 89.
Case 34232 (Rec. Mass. Gen. Hosp.) (1948), *New Engl. J. Med.*, **238**, 812.
DAVIS, J. S. (1908), *Johns Hopk. Hosp. Bull.*, **19**, 74.
— — and KITLOWSKI, E. A. (1930), *Arch. Surg. Chicago*, **20**, 39.
FORCONI, P., and FICAI, A. (1948), *G. ital. Chir.*, **4**, 347.
FULTON, M. N., and SOSMAN, M. C. (1942), *J. Amer. med. Ass.*, **119**, 319.
GEREMIA, B., and FANZAGO, G. (1952), *Riv. Anat. Pat. Onc.*, **5**, 623.
GIBB, W. P. (1913), *Brit. med. J.*, **1**, 74.
HAARDT, W. (1953), *Mschr. Ohrenheilk.*, **87**, 227.
JENKINS, H. D., and DELANEY, P. A. (1932), *Surg. Gynec. Obstet.*, **55**, 464.
JONES, K. G. (1953), *J. Bone Jt Surg.*, **35**, 717.
LAZAR, D. (1947), *Orv. Lapja.*, **3**, 1486.
LIGHT, R. A. (1943), *Ann. Surg.*, **118**, 465.
LISTON, R. (1843), *Med-chir. Trans.*, **26**, 120.
MAILER, R. (1935), *Brit. J. Surg.*, **23**, 245.
MASSERA, L. (1947), *Ateneo parmense*, **18**, 255.
— — (1949), *Arch. ital. Chir.*, **71**, 162.
PELIZZOLO, G. (1953), *Tumori*, **39**, 47.
PERUSI, A. (1951), *Arch. Ortop. Milano*, **64**, 55.
POMERANZ, M., and TUNICK, I. S. (1941), *Ann. Surg.*, **114**, 1050.
PUPILLI, F. (1951), *Friuli med.*, **6**, 557.
RUSSOLILLO, M. (1951), *Rif. Med.*, **65**, 293.
SCHEUER, F. (1952), *Z. orthopäd. Chir.*, **81**, 640.
SHALLOW, T. E., EGER, S. E., and WAGNER, F. B. (1944), *Ann. Surg.*, **119**, 700.
STOUT, A. P. (1943), *Ibid.*, **118**, 445.
UBERTI, E. (1953), *Minerva Chir.*, **8**, 63.
WAKELEY, CECIL P. G. (1921), *Arch. Radiol. Electrother.*, **25**, 363.
WATSON, W. L., and MCCARTHY, W. D. (1940), *Surg. Gynec. Obstet.*, **71**, 509.
WEAVER, J. B., and RUMOLD, M. J. (1943), *Amer. J. Surg.*, **60**, 149.
WILLIS, R. A. (1953), *Pathology of Tumours*, 700. London: Butterworth.

SPIGELIAN HERNIA

REPORT OF FIVE CASES AND REVIEW OF THE LITERATURE

By DAVID BAILEY

FIRST ASSISTANT, SURGICAL UNIT, UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

SPIGELIAN hernia, although not rare, is not a commonly recognized condition and receives scant attention in most of the standard text-books. River (1942) reviewed 116 cases, including 4 of his own, and since that time an increasing number have been reported, but only 29 of these are in the British and American literature.

Cotter (1946) suggests that the hernia is probably more common than is generally thought and that its recognition may be important as an occasional cause of abdominal pain.

During the last two years, 4 cases have been seen personally at University College Hospital. These are reported together with a further case from the surgical records of the hospital.

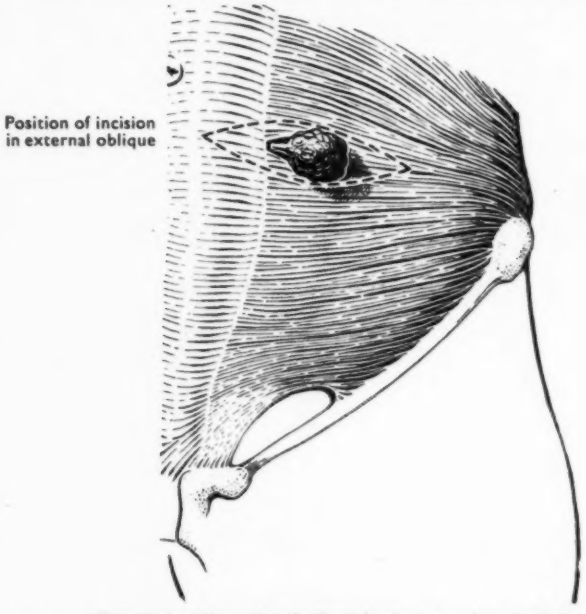


FIG. 630.—Operative findings in *Case* 1. A pedunculated lobulated mass of extraperitoneal fat protrudes through a split in the fibres of the internal oblique.

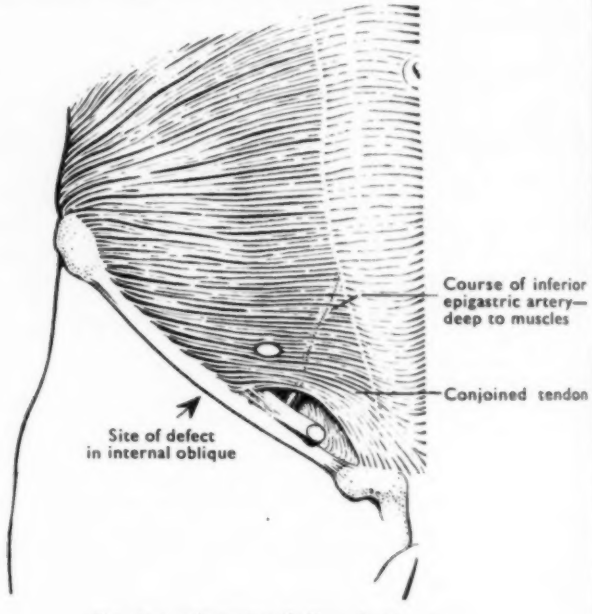


FIG. 631.—Operative findings in *Case* 3.

CASE REPORTS

Case 1.—A male greengrocer, aged 61 years, was admitted on July 12, 1953. One year previously he first noticed pain in the left groin and shortly afterwards found a lump there. The pain was brought on by lifting and relieved by pressure with the hand and also by lying down. In addition to the local pain he had also experienced several attacks of intermittent pain in the upper abdomen.

ON EXAMINATION.—A rather fat, but otherwise healthy, man. There was a visible and palpable lump situated in the left iliac fossa at the level of the anterior superior iliac spine and about halfway between it and the midline. There was an expansile impulse on coughing and the swelling reduced on lying down, but a rather indefinite residuum could still be palpated. There was also a small para-umbilical hernia.

AT OPERATION.—The lump was found to be deep to the intact external oblique and, after incision of this layer, a lobulated mass of fat (6×4 cm.) was exposed (*Fig.* 630). This proved to be pedunculated, the stalk protruding through a split between the fibres of the internal oblique just lateral to the edge of the rectus muscle. On dissection the mass of fat was found to contain a hernial sac the neck of which passed through an opening in the transversus aponeurosis about 1 cm. in diameter. The sac contained omentum; this was reduced and the neck closed with a catgut ligature. The gap in the transversus and internal oblique was closed with interrupted catgut sutures. The external oblique and skin were repaired with interrupted silk.

Case 2.—A woman of 79 years was first seen on Aug. 14, 1954. She complained of a lump in the left side of her abdomen which had been coming and going at intervals for many years. There was no local pain, but the appearance of the lump was accompanied by violent pain in the upper abdomen which was not relieved until she was able to push the lump back. Twenty years previously a gynæcological operation had been carried out through a lower midline incision.

ON EXAMINATION.—She was a thin, senile woman. A mass 8 cm. in diameter was situated in the left iliac fossa at the level of the anterior superior iliac spine. There was a well-marked cough impulse, and reduction of the mass, which was not easy, was accompanied by a gurgle. The lower median incision was sound.

AT OPERATION.—The findings were similar to those in *Case* 1, except that the sac contained small intestine and omentum, and a large vessel was seen in close relation to the medial side of the neck of the sac. The neck of the sac was situated at the edge of the rectus about 8 cm.

above the pubis. The adherent omentum was resected and the neck of the sac ligated with catgut. The transversus and internal oblique were overlapped and repaired with mattress sutures of thread after the manner of the Mayo repair of an umbilical hernia.

Case 3.—A male scientific instrument maker, aged 46 years, was admitted to hospital on Nov. 8, 1954. He complained of a lump in the right groin first noticed about seven months previously. Attention was drawn to the lump by a persistent dull ache, worse on standing or lifting. He also suffered from occasional attacks of 'wind' in the stomach, had recently become constipated, and had had to start taking aperients.

ON EXAMINATION.—He was a thin man. On coughing there was a diffuse bulging in the region of the right inguinal canal, but no hernia could be palpated at the external ring. On standing a more definite lump could be felt about 4 cm. above and lateral to the pubic tubercle. Sigmoidoscopy and a barium enema were negative. He was thought to have a small indirect inguinal hernia and, in view of his symptoms, operation was advised.

AT OPERATION.—No inguinal hernia was discovered, but a small hernial sac covered by extraperitoneal fat was seen emerging between the fibres of the internal oblique about 2·5 cm. above and just medial to the internal ring. The neck of the sac lay above and lateral to the inferior epigastric vessels (*Fig.* 631). The neck of the sac was isolated and ligated after opening, the aperture in the internal oblique and transversus being closed with interrupted catgut sutures. The repair was reinforced with a flap of rectus sheath.

Case 4.—A housewife of 58 years was admitted to hospital on Nov. 28, 1954 complaining of a dragging feeling in the left lower abdomen for five to ten years. This had been worse during the last six months and she had been conscious of a lump there. She had also suffered occasional spasms of sharp pain in the same place.

ON EXAMINATION.—She was short and very fat. An indefinite swelling was felt in the left iliac fossa about halfway between the midline and the anterior superior iliac spine. This was obscured by the overlying fat, but could be felt more easily with the patient standing and tensing the abdominal muscles. It was slightly tender; there was no cough impulse and it was not reducible.

A diagnosis of Spigelian hernia was thought most likely, but a lipoma of the abdominal wall was also considered. She was also found to be suffering from diabetes.

AT OPERATION.—A transverse incision was made over the lump. The findings were almost exactly similar to those in *Case* 1. The mass of extraperitoneal fat measured 8 × 5 cm. and the neck of the sac, which was situated at the lateral border of the rectus about 4 cm. above the pubic tubercle, measured 1·5 × 0·5 cm. The hernia was repaired with overlapping of the muscle layers as in *Case* 2. In this case marked banding of the fibres of the internal oblique was noted.

Case 5.—A female tea-bar attendant, aged 44 years, was admitted to hospital on May 10, 1935. She complained of a lump in the right lower quadrant of her abdomen first noticed six years previously when scrubbing a floor. She was conscious of an aching pain on standing; the lump disappeared and the pain was relieved on lying down.

ON EXAMINATION.—She was a thin woman. A soft swelling 3 cm. in diameter was found just below McBurney's point. There was an expansile cough impulse and the lump was reducible; after reduction a gap about 2 cm. across was felt in the abdominal wall. No other abnormality was found.

AT OPERATION.—A pararectal incision was made over the swelling. There was a wide split in the internal oblique at the edge of the rectus sheath, through which a small peritoneal sac covered by transversalis fascia protruded. The aponeurosis of the external oblique was thin but intact. The sac was opened and found empty. The cæcum was delivered and the appendix removed. The edges of the sac were excised at the neck and the peritoneum was repaired. The internal oblique was repaired with overlapping with mattress sutures of interrupted thread. The external oblique was similarly repaired.

DISCUSSION

Nomenclature.—This hernia has been given a variety of names. 'Spigelian hernia' appears to be the most popular, but for those who dislike eponymous titles 'hernia in the linea semilunaris', 'interstitial hernia of the linea semilunaris', and 'spontaneous lateral ventral hernia' are alternatives. These names should only be used for spontaneous herniæ.

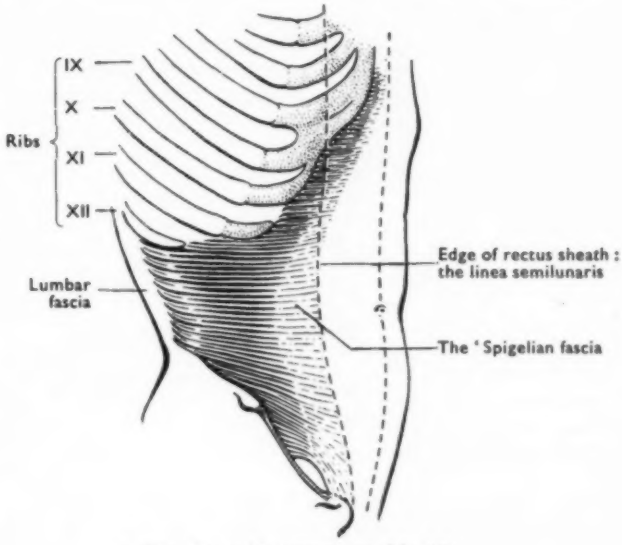


FIG. 632.—*M. transversus abdominis.*

Historical.—The linea semilunaris was first described by Adrian van der Spiegel (1578–1625), Professor of Anatomy and Surgery in the University of Padua (Bailey and Love, 1949; Sheehan, 1951). Laterally situated ventral hernia was described by La Chausse in 1746 (Holloway, 1922), but was considered to be traumatic in origin, and the first clear description was given in 1764 by Klinkosch (River, 1942), who was the first to use the present title. Sir Astley Cooper recognized the hernia and reported 3 cases in 1807 (Cooper, 1807).

Anatomy and Definition.—Anatomically the linea semilunaris is a curved groove extending from the tip of the 9th costal cartilage to the pubic spine marking the outer border of the rectus abdominis (*Gray's Anatomy*, 1949). In previous reports there appears to be some difference of opinion as to what exactly constitutes Spiegel's line. Watson (1948) defines it as the line which represents the point of division of the internal oblique aponeurosis to enclose the rectus muscle. River (1942) defines it as the line of transition between the muscle bundles and aponeurosis of the transversus. This lies for the greater part at some distance lateral to the edge of the rectus sheath, but the muscle-fibres of the internal oblique extend right up to the edge of the sheath.

These points have been verified many times during the course of the gridiron approach to the appendix (*Fig.* 633).

Holloway (1922) notes that the 'line' is, in reality, a broad band, and Aird (1949) refers to the 'Spigelian fascia', indicating this as the aponeurosis

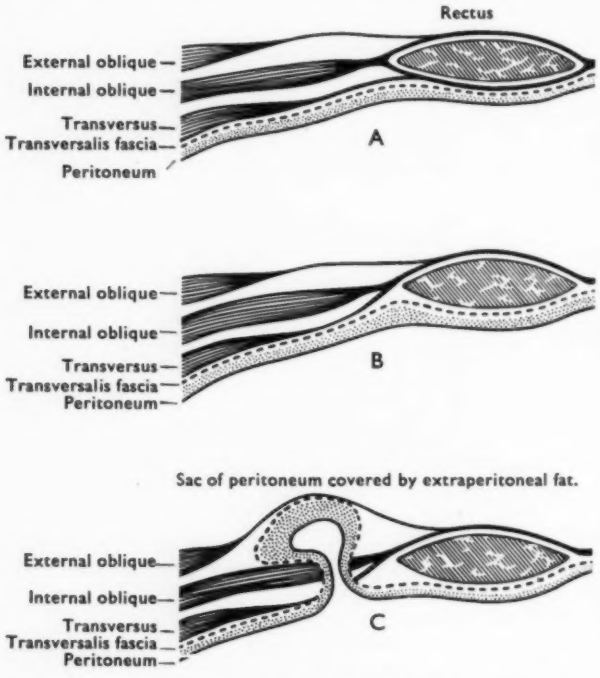


FIG. 633.—Cross sections of abdominal wall. A, above the arcuate line (of Douglas); B, below the arcuate line; C, Spigelian hernia below the arcuate line.

separating the muscular part of the transversus from the edge of the rectus sheath. A good working definition of a 'Spigelian hernia' is a hernia which protrudes through the 'Spigelian fascia'. Certainly not all reported cases lie in the anatomical linea semilunaris (*Fig.* 632).

The majority of reported cases lie below the umbilicus, although exceptions have been described (Wakeley and Childs, 1951; Koontz, 1952), and most authorities agree that the commonest site is at the level of the semilunar fold of Douglas, a structure which is situated at a variable distance below the umbilicus (Perrigard, 1947; Mastics, 1954). The rarity of this hernia in the upper abdomen is to be expected, as in the majority of subjects the muscle-fibres of the transversus reach behind the rectus in this region.

Morphologically many direct inguinal herniæ are herniæ through the linea semilunaris below (and medial) to the inferior epigastric vessels, but there does not seem to be any useful purpose in including this more common variety under the heading of Spigelian hernia. Perrigard (1947), however, differentiates the superior and inferior semilunaris herniæ according to their relation to the inferior epigastric vessels.

It is not clear whether the hernia described by Cattell and Aronoff (1944) should be considered under this heading, but those described as para-inguinal by Grierson and Leacock (1949) are probably similar to our *Case* 3 and represent low-sited Spigelian herniæ. The unusual hernia entering the rectus sheath (Mastics, 1954) is clearly different.

The *margins* of the defect in the Spigelian fascia are rigid and sharp and the defect usually varies from 0·5 cm. to 2 cm. in diameter (Bryant, 1947), although larger apertures have been described (Larson, 1951). The hernia, covered with extra-peritoneal fat, then expands like a mushroom to lie between the internal and external obliques. (*Fig.* 633 C.) The sac itself is usually comparatively small, but very large ones have been reported (Paul and Hill, 1943; Larson, 1951). The peritoneal sac is sometimes covered by transversalis fascia (Mason and Ruge, 1948) and this was noted in *Case* 5.

Small intestine and omentum are the most common *contents* but the large intestine may be involved (Coley, 1909; Wakeley and Childs, 1951; Straus and Alexander, 1953). Belluzzi (1950) has reported a hernia containing stomach, and sliding herniæ have been described by River (1942) and Bryant (1947).

Strangulation is common, probably owing to the small rigid neck (Cooper, 1807; Watson and Scotter, 1951) and some Richter's herniæ have been reported (Sheehan, 1951).

Age and Sex Incidence.—Spigelian herniæ have been reported in patients as young as 10 years (Paul and Hill, 1943) and as old as 80 years (Koontz, 1952). The majority have been diagnosed in the fifth and sixth decades and are approximately equally divided between males and females. The most typical sufferer is the "corpulent gentleman advanced in years", described by Sir Astley Cooper (1807). These herniæ are frequently associated with more common varieties and bilateral Spigelian herniæ were reported by Berger in 1918 (Holloway, 1922).

Aetiology.—Sir Astley Cooper (1827) described the predisposing causes of hernia in general as obesity, repeated pregnancy, great wasting of the body, injury, violent exercise, flatulent food, and food difficult of digestion. To these we may add chronic cough and the presence of ascites.

With reference to Spigelian hernia, Cooper (1804) mentioned the part played by vessels perforating the linea semilunaris, and the importance of these vessels has frequently been emphasized (Robinson, 1914), although others deny that they are a contributing factor. In some cases, as in our *Case* 2, vessels have been noted in close association with the neck of the sac (Wakeley and Childs, 1951). Congenital defects of the abdominal wall are occasionally responsible for the hernia, as in the case described by Paul and Hill (1943).

The most attractive hypothesis to account for these herniæ is that advanced by Zimmerman and his associates (Zimmerman, Anson, Morgan, and McVay, 1944). They have pointed out that the conventional description of the internal oblique and transversus muscles is not always correct and that instead of the muscular portions consisting of strata of evenly distributed fascicles, they may consist of separate musculo-aponeurotic bands held together by the internal and external investing fascial layers. By careful dissections they have demonstrated this 'banding' in a high percentage of abdominal walls

and in 10 per cent they showed that the defects between the bands of the internal oblique and transversus were superimposed upon one another, thus providing a potential weakness. Furthermore, they have shown that these defects are common in the region of the semilunar fold of Douglas, accounting for the common site for the hernia. In fat subjects these gaps between the musculo-aponeurotic bands are further weakened by the deposition of fat; this may explain the frequent association of the hernia with obesity. These bands were well marked in our *Case* 4.

The part played by the extraperitoneal fat has also been stressed by many authors (Sarot, 1941); it appears that the fat acts as a wedge, finding out the weak spots and pulling a cone of peritoneum behind, as in the formation of an epigastric hernia.

Diagnosis.—Probably the most important thing about making the diagnosis is to bear the condition in mind (Sarot, 1941) and the importance of Spigelian hernia as an occasional cause of pain in the right iliac fossa has been stressed by Reid (1949). In most of our cases the diagnosis of hernia was obvious, but it was somewhat obscure in *Case* 4 and only familiarity with the condition suggested it.

The symptoms may be either referred or local (Sheehan, 1951). The former are those of intestinal obstruction and, if the presence of a Spigelian hernia is not recognized, the cause may only be discovered at laparotomy. The chief local symptom is pain or discomfort. It is usually well localized and is made worse by coughing, straining, or standing for a long time; it may be severe, but is sometimes only a feeling of 'something there that shouldn't be' (Wakeley and Childs, 1951). On occasions the pain is of a more diffuse neuralgic type or may amount to no more than a vague dyspepsia. Macewen (1907) suggests that some of the pain may be due to distension of the narrow neck causing pressure on, and irritation of, peripheral nerves, but this has not been clearly demonstrated. Frequently the pain is accompanied by a sensation of gurgling (Coley, 1909; Bryant, 1947), and it may be relieved by pressure with the hand, as in *Case* 1. It is characteristic that the symptoms are out of all proportion to the size of the hernia, as with the more common epigastric type. Besides the pain the patient is sometimes aware of a lump which comes and goes, and this may be the presenting symptom.

On examination the typical physical signs of a hernia may be present, but, if the patient is fat and the hernia small, only an indefinite lump may be found, sometimes no more than a mere thickening on deep palpation (Robinson, 1908). Rarely there is only local tenderness without a lump, and in this event the diagnosis is likely to be difficult. The mass of extraperitoneal fat associated with the sac may be a help in diagnosis provided it is not mistaken for a simple lipoma, but the hernia may be masked by the intact external oblique. In our experience diagnosis is most easily made if the patient is examined standing with the muscles tensed, or lying supine and raising the head and shoulders from the couch; this latter procedure excludes visceral tenderness in difficult cases (River, 1942). The examiner may feel a defect in the abdominal wall after reduction of the hernia, as in *Case* 5. The importance of repeated examinations is stressed by Macewen (1907), as the hernia may not be found on the first occasion. The hernia is sometimes discovered at operation for some other condition (Brosnan, 1949; Koontz, 1952), and the neck of the sac may then be felt from within. Radiology has little to offer in the diagnosis, but rarely the nature of an obscure swelling has been made clear as the result of a barium enema (Straus and Alexander, 1953), or barium meal (Mason and Ruge, 1948).

Differential Diagnosis.—The symptoms due to Spigelian hernia have often been attributed to intra-abdominal disease. Cases have been reported which simulated acute appendicitis (Sarot, 1941; Reid, 1949), appendix abscess (Robinson, 1908), stone in the bladder (Watson, 1948), and liver disease following cholecystectomy (Watson and Scotter, 1951). If there is no cough impulse a tumour of the abdominal wall (Sheehan, 1951; Mersheimer, Winfield, and Ruggiero, 1951), or a spontaneous hæmatoma of the rectus sheath (Cullen, 1937) may be diagnosed. Sometimes a Spigelian hernia may be confused with some other variety of hernia (Brosnan, 1949; Mastics, 1954), as in our *Case* 3. If the hernia is unrecognized the patient may even be suspected of malingering (Watson, 1948).

Treatment.—Although the symptoms may be relieved by wearing a tight abdominal belt (Holloway, 1922), it is clear that the risk of strangulation is high and surgery should be undertaken without delay. Sir Astley Cooper (1807) described taxis and treatment by truss, but these practices are now condemned.

The hernia is best exposed by a transverse incision over the lump and division of the external oblique. The neck of the sac is dissected out and ligatured or sutured with catgut, the overlying muscles being repaired with interrupted sutures. If desired, these may be overlapped as in the Mayo repair of an umbilical hernia. Only occasionally, in large herniæ, is reinforcement with fascia required.

I have not found any cases of recurrence reported.

SUMMARY

1. Five cases of Spigelian or spontaneous lateral ventral hernia are reported.

2. The anatomy is discussed. There is some confusion in the literature as to the exact definition of the hernia, but in these 5 cases the neck was situated in the Spigelian fascia, corresponding to that part of the aponeurotic portion of the transversus which lies lateral to the rectus sheath. The majority have narrow necks and lie below the umbilicus.

3. The aetiology is discussed. Banding of the transversus and internal oblique is considered the main predisposing factor.

4. The signs and symptoms are described. The lump may be difficult to find and the diagnosis therefore obscure.

5. Surgical repair is required for the relief of pain and because of the high incidence of strangulation.

I would like to thank the members of the Surgical Staff of University College Hospital for permission to publish these cases.

I am also grateful to Mr. V. K. Asta, the medical artist of University College Hospital Medical School, who drew the figures.

REFERENCES

AIRD, I. (1949), *A Companion in Surgical Studies*, 536. Edinburgh: E. & S. Livingstone.
BAILEY, H., and LOVE, R. J. M. (1949), *A Short Practice of Surgery*, 8th ed., 481. London: H. K. Lewis.
BELLUZZI, V. (1950), *Policlinico. Sez. prat.*, **57**, 1151.
BROSNAN, G. (1949), *Med. J. Aust.*, **1**, 617.
BRYANT, A. L. (1947), *Amer. J. Surg.*, **73**, 396.
CATTELL, R. B., and ARONOFF, B. L. (1944), *Surg. Clin. N. Amer.*, **24**, 731.
COLEY, W. B. (1909), *Ann. Surg.*, **50**, 246.
COOPER, Sir A. (1804), *The Anatomy and Surgical Treatment of Inguinal and Congenital Hernia*, 1. London: T. Cox.
— — (1807), *The Anatomy and Surgical Treatment of Hernia*, pt. II, 58. London: Longman, Hurst, Rees & Orme.
— — (1827), *Lectures on the Principles and Practice of Surgery*, vol. III, 14. London: Simpkin and Marshall.
COTTER, W. M. (1946), *N.Z. med. J.*, **45**, 240.
CULLEN, T. S. (1937), *Bull. Johns Hopk. Hosp.*, **61**, 317.
Gray's Anatomy (1949), 30th ed., 581. London: Longmans, Green & Co.
GRIERSON, J., and LEACOCK, A. (1949), *Brit. J. Surg.*, **36**, 327.
HOLLOWAY, J. K. (1922), *Ann. Surg.*, **75**, 677.
KOONTZ, A. R. (1952), *Ibid.*, **135**, 875.
LARSON, E. E. (1951), *Amer. J. Surg.*, **82**, 103.
MACEWEN, J. A. C. (1907), *Lancet*, **2**, 1081.
MASON, M. L., and RUGE, D. (1948), *Quart. Bull. Northw. Univ. med. Sch.*, **22**, 71.
MASTICS, E. A. (1954), *Ohio St. med. J.*, **50**, 676.
MERSHEIMER, W. C., WINFIELD, J. M., and RUGGIERO, W. F. (1951), *Arch. Surg. Chicago*, **63**, 39.
PAUL, M., and HILL, W. C. O. (1943), *Brit. J. Surg.*, **30**, 385.
PERRIGARD, G. E. (1947), *Canad. med. Ass. J.*, **57**, 575.
REID, D. R. K. (1949), *Brit. J. Surg.*, **36**, 433.
RIVER, L. P. (1942), *Ann. Surg.*, **116**, 405.
ROBINSON, H. B. (1908), *Brit. med. J.*, **2**, 781.
— — (1914), *Brit. J. Surg.*, **2**, 336.
SAROT, I. A. (1941), *J. Mt Sinai Hosp.*, **8**, 164.
SHEEHAN, V. (1951), *J. Irish med. Ass.*, **29**, 87.
STRAUS, F. H., and ALEXANDER, M. J. (1953), *Illinois med. J.*, **103**, 353.
WAKELEY, Sir CECIL, and CHILDS, P. (1951), *Lancet*, **1**, 1290.
WATSON, D., and SCOTTER, B. (1951), *Brit. med. J.*, **1**, 74.
WATSON, L. F. (1948), *Hernia*, 3rd ed., 368. London: H. Kimpton.
ZIMMERMAN, L. M., ANSON, B. J., MORGAN, E. H., and MCVAY, C. B. (1944), *Surg. Gynec. Obstet.*, **78**, 535.

THE TREATMENT OF RECURRENT CARCINOMA OF THE RECTUM BY SUPERVOLTAGE X-RAY THERAPY

BY IVOR G. WILLIAMS, IVOR M. SHULMAN, AND IAN P. TODD

THE problem of treatment of carcinoma of the rectum is seldom that of the primary tumour, which is surgical, but rather that of recurrences or metastases which are rarely, if ever, amenable to excision. In the past radium and medium X-ray therapy (250 kv. range) have been tried and found disappointing in their results, both in alleviation of symptoms and attempted cure of the disease. Ralston Paterson in 1948 categorically stated of rectal cancer: "Carcinoma recurrent post-operatively cannot be successfully treated by any known radiological method." We would agree with this statement as far as a high cure-rate is concerned. Experience, however, with X rays generated at very high voltages, one million volts and over, shows that supervoltage X-ray therapy has a very definite place in the primary treatment of advanced adenocarcinoma of the rectum as well as in the treatment of recurrent disease.

Carcinoma of the rectum is inherently radioresistant. In view of the 5 per cent of 5-year cure-rate of cases deemed inoperable by the surgeons of St. Mark's and St. Bartholomew's Hospitals, and our experience with 82 cases of recurrent rectal carcinoma treated by this method and analysed in this paper, we believe that some types are radiosensitive and alleviation of pain and other symptoms can be obtained in such a large proportion of cases as to make the treatment worth while.

Mode of Reference of Cases.—The present series consists of 82 cases of carcinoma of the rectum which recurred after surgical treatment of the primary. Of these, 52 were referred from the surgeons of St. Mark's Hospital and 30 from St. Bartholomew's Hospital. There were 43 females and 39 males.

Modes by which Patients presented Themselves.—The commonest symptom of recurrent neoplasm was pain, and in many patients at this stage no signs may be detectable to indicate the cause and source of this pain. From our experience this symptom must always be regarded as highly suspicious of recurrence, for later either a mass, or radiological or neurological evidence, will become apparent. The cause of the pain may sometimes be obvious on clinical examination and growth may be felt in the pelvis or abdomen, or radiology may disclose a metastasis in the bones of the pelvis or lumbar spine.

A careful neurological examination should be carried out to localize as accurately as possible the site of the lesion. If pain is of bony origin, it is either due to stretching of the periosteum over the metastasis, when it is usually boring and severe in character, or it is due to destruction of bone substance, when it is less well-defined and aching in character. There may be a localized tenderness to pressure. If nearby sensory nerves are involved pain may be referred to the related cutaneous areas. This pain may become of great severity, being lancinating and intermittent, but it is usually preceded by a period of hyperæsthesia of the skin to light touch. Soft-tissue metastases usually occur within the field

of the surgical procedure. Pain referred from these metastases is usually aching in character but varies in its intensity. Its distribution depends upon the situation of the metastasis and the structures involved. Pain may also arise in scar tissue which involves spinal nerves and need not necessarily be due to metastasis. Indeed, when clinical examination is negative, it is impossible to distinguish between the pain of metastatic growth and pain due to scar tissue, as anatomically the same nerve pathways are involved and the pathological process is essentially the same.

From our experience, however, deep-seated pain following excision of the rectum for malignant disease has been found generally to be of metastatic origin. This fact is strengthened by the comparative absence of pain following removal of the rectum for benign conditions such as uncomplicated ulcerative colitis.

In the present series there were 49 patients complaining of pain as the presenting symptom. In the main this pain occurred in one of three situations, the perineum, the lumbar region, and the leg. Perineal pain is often described as "where the rectum used to be". In these cases the metastasis is deep seated. If cutaneous or subcutaneous nodules can be felt, there is more superficial tenderness and pain. In our series there were 28 cases of this type.

Back pain occurred in 11 cases as the presenting symptom. It is most commonly a nagging ache and situated in the small of the back. This may be due to soft-tissue or bony metastasis, but it must be remembered that metastases in bone can cause pain before radiological evidence is demonstrable.

Leg pain is usually sciatic in character but may be referred to any area supplied by the lumbosacral plexus. This pain is usually severe in character and can rarely be controlled by analgesics. However, relief of pain can be accomplished by supervoltage X-ray therapy in a large number of these patients. In our series there were 10 patients who presented with 'sciatica'.

The presenting symptom is seldom anything other than pain, although a mass is frequently present. This occurred in 37 cases, and whilst it may occasionally be found by the patient, it is more often found at clinical examination, particularly in the female where pelvic examination is still possible.

Table I shows the diversity of less-frequent presenting symptoms and signs.

Table I.—Less Frequent Presenting Symptoms

Glandular enlargement	10
Discharge	13
Bleeding	4
Leg swelling	1
Diarrhœa	1
Urinary	3
Perineal abscess	1
Unspecified	2
No symptoms	6

Discharge occurred mainly after perineal excision of the rectum, where it is a common sequel even without recurrence.

The Aims of Treatment.—In the early small localized recurrences an attempt at radical cure was made. When the recurrence was more widespread locally or presented as a metastasis, either in soft tissue or bone, palliative treatment to relieve symptoms was carried out. Before radical treatment was attempted a full clinical and radiological examination of the patient was performed to exclude any distant metastases.

Where radical therapy was employed the aim was to deliver a dose of 6000 r in six weeks, and this was achieved in the greater percentage of cases treated. In a small minority of cases severe skin reaction in the groins and perineum resulted in curtailment of treatment at a lower dosage level. Treatment was always extended to the limit of tolerance. Factors causing interruption in the treatment were radiation enteritis, colitis, and cystitis, since in a planned attack on the recurrent growth the small bowel, colon, and bladder, of necessity receive exposure owing to their position in the pelvis on which the planned X-ray beams converge.

In female patients vulvitis and vaginitis are troublesome but seldom of sufficient intensity to interrupt treatment for more than a day, if at all.

Some patients have mild general radiation effects, but this is seldom more than nausea.

In the cases treated palliatively for the relief of symptoms a simple arrangement of fields is used. Dosage level is in the region of 3000–4000 r fractionated over three to four weeks. In the greater proportion of cases this gives good relief of pain for several months and makes the patient's remaining life more comfortable and the very difficult problem of terminal care shorter and easier.

METHODS OF TREATMENT

X rays generated at 1000 kv. were employed in all our cases. Two advantages of X rays at this kilovoltage over the conventional 250-kv. X rays are a more homogeneous distribution of radiation to the volume treated and a far superior skin-depth dose ratio, with resultant diminution in the severity of the skin reaction. At supervoltage X-ray level there is no differential absorption in bone, as occurs at 250 kv.

A full clinical and radiological examination of the patient is performed before deciding on treatment. At planning, a section of the body containing the volume decided upon for treatment is taken, after careful assessment of the involved volume of tissue. This is of great importance in order to achieve the greatest benefit from treatment and also to utilize to the maximum the very small differential tissue/tumour tolerance. Isodose charts are drawn up in all cases radically treated, and this usually entails using four or five fields, 15–20 cm. long and 7–10 cm. wide, two anterior oblique, two posterior oblique, and a direct posterior field being a typical selection. Depth dose in the region of 150 per cent is attained with this distribution of fields. The fields are so selected and angled as to avoid any X-ray beam passing directly through the hip-joint, thus obviating avascular necrosis and femoral neck fracture, which has never occurred in any of our cases. Every patient is considered as an individual problem and a decision is made and a proper balance struck as to the ultimate probable benefit to be gained by treatment. The treatment is lengthy—six weeks—and it is important to keep the morale of the patient high. Treatment is carried out daily except at week-ends. Every case is carefully assessed daily

by the medical officer and any undue reactions are noted and acted upon either by diminishing the daily dose or by interrupting treatment. Great care is taken by good nursing to keep skin reactions down to the minimum. 'Pyridoxine' or 'Avomine' is given for the occasional generalized radiation reaction. Blood-counts are performed at 5-day intervals, but only rarely does anæmia, leucopenia, or thrombocytopenia interrupt treatment.

General measures include care of hydration, and an easily assimilated high-calorie protein diet is given. Post-radiation depression may necessitate a suitable drug. Pain in the early stages requires medication, but usually improves after about ten days. Transfusion has been employed for severe anæmia when this was indicated. In palliative treatment for relief of symptoms simple field arrangements are used and undue reactions are avoided.

RESULTS

It must be remembered that the primary object of treatment with supervoltage X rays is to alleviate symptoms, and only rarely can an attempt at cure be made. In spite of this, out of 82 cases treated 8 are alive, one 11 yr., one 8 yr. 3 mth., one 4 yr. 10 mth., one 4 yr. 6 mth., one 2 yr. 8 mth., one 2 yr., one 1 yr. 8 mth., and one 1 yr. after treatment.

Table II.—Relief of Symptoms

Periods of Relief of Symptoms months	*No. of Patients*
0–3	33
4–6	17
7–9	5
10–12	10
13–15	1
16–18	4
31–33	1
46–48	2
70–72	1

In the remaining 74 patients symptoms were fully alleviated for an average of 7·7 mth.

Table II shows the distribution of relief in 3-monthly periods. These patients survived an average of 12·75 mth. after completion of treatment.

Table III.—Periods of Survival

Periods of Survival months	*No. of Patients*
0–3	13
4–6	16
7·9	7
10 12	11
13·15	7
16·18	10
22 24	4
31·33	2
34 36	1
46–48	1
58–60	1
70–72	1

Table III shows the distribution of survival in 3-monthly periods.

There appears to be no significant difference in the interval between primary operation and the symptoms or signs of recurrence when correlated with the grade of malignancy of growth nor with its 'Dukes Grading' (A, B, C, and C_2). This fact appears illogical, for it is known that high-grade cases have a poor prognosis. Furthermore, the site in the rectum of primary growth (upper, middle, or lower third) does not in our series appear to influence the incidence of recurrence. We can offer no explanation for this.

SUMMARY

A series of 82 cases of recurrent carcinoma following surgical removal of the rectum is presented. The object of treatment was to alleviate symptoms. Figures are given which show that this aim is achieved. Out of 82 cases, 8 (10 per cent) survive—3 yr. and over in 4 patients, and 4 patients are alive and well 32, 24, 20, and 12 mth. after treatment. Of the 82 cases 71 (86·6 per cent) benefited from treatment; 11 (13·4 per cent) showed no real improvement of symptoms.

In spite of the fact that six weeks are spent on the treatment and that dosage level is high, details of which are given, only 3 cases suffered more than the expected irradiation reaction (2 radionecrosis and 1 radiodermatitis).

Pain was the predominant symptom and an account has been given of its type and site and distribution.

CONCLUSION

Supervoltage X-ray therapy has a well-defined place in the treatment of recurrent carcinoma of the rectum because it relieves symptoms.

Recurrent carcinoma of the rectum can seldom, if ever, be treated by surgery, apart from neurosurgical methods. The symptom of pain in its various types and sites heralds recurrence, though no signs may be present. It is at this stage that supervoltage X-ray therapy should be exhibited energetically, on the fundamental radiotherapeutic principle that the best results are obtained when the involved volume of tissue is small.

Furthermore, if for any reason the surgeon is not satisfied with the excision, or the pathological report shows extensive local spread or a high grade of malignancy, in spite of the fact that in our series there was no correlation between grade of malignancy, site of growth, and interval of recurrence, we feel that an immediate post-operative course of supervoltage X-ray therapy offers the best chance of a cure. This is perhaps even of greater importance in the younger patient, in whom the prognosis is known to be poor.

REFERENCES

Cade, Stanford (1952), *Malignant Disease and its Treatment by Radium.* Bristol: Wright.

Paterson, Ralston (1948), *The Treatment of Malignant Disease by Radium and X-rays.* London: Arnold.

Williams, I. G., and Morgan, C. Naunton (1955), *British Practice in Radiotherapy.* London: Butterworth.

RHABDOMYOSARCOMA OF THE HAND FOLLOWING SEVERE TRAUMA

By R. J. R. CURETON and J. D. GRIFFITHS

FROM THE DEPARTMENT OF PATHOLOGY AND PROFESSORIAL SURGICAL UNIT, ST. BARTHOLOMEW'S HOSPITAL

MALIGNANT mesodermal tumours occurring in the hand are uncommon neoplasms, only three such cases being recorded among 96 soft-tissue sarcomas treated at this hospital from 1947–1955 inclusive. One of these was a fibrosarcoma, one a malignant synovioma, and the present case a rhabdomyosarcoma which arose in the adductor pollicis muscle.

Tumours containing primitive voluntary muscular elements are found most commonly as 'embryonic' tumours occurring in the urogenital tract, or as part of a teratoma. Tumours arising from the skeletal musculature are rare and, as they may be mistaken for acute inflammatory conditions, are of some surgical interest.

The relationship between injury and the subsequent development of a neoplasm has always been a debatable issue and, in view also of certain diagnostic difficulties experienced with these tumours, it seems worth recording the following case, in which an undoubted rhabdomyosarcoma developed, in the hand of an adult, nine years after a severe crush injury.

CASE REPORT

HISTORY.—J. K., a man aged 33 years, attended hospital complaining of a swelling in the right hand. For three weeks he had noticed this developing in the palm; it was painless and gave rise to no symptoms or disability.

Nine years previously he had sustained a crush injury to his right hand at work and was admitted to hospital with contusion of the hand and a fractured scaphoid, associated with a disarticulation of the trapezoid. Following two months in plaster, it was found that there was a weakness of the thenar muscles, which was attributed to a median nerve palsy. After physiotherapy for over two years the muscles recovered, leaving only slight residual weakness in the affected muscles. He had a good functional hand and was able to continue his occupation in the catering trade. He was in good health and did not complain of any symptoms.

ON EXAMINATION.—The man looked well, and his temperature and pulse were normal. There were no abnormal physical signs in his chest, heart, or abdomen. There were small soft lymph-nodes palpable in both axillæ. In the right hand there was a round swelling, measuring about 7·5 cm. in diameter, arising from the deep tissue of the palm on the ulnar side of the thenar eminence. The lesion occupied the first interosseous space, passing backwards between the first and second metacarpals into the anatomical snuff-box. The swelling was soft in consistency, but there was no fluctuation or transillumination in the region. The skin over the area was normal in colour, but there was local increase in temperature. Sensation was normal all over the hand. All active movements of the hand were full except for opposition, which was limited owing to the bulk of the tumour in the palm preventing the approximation of the thenar and hypothenar eminences. There was no wasting of the intrinsic muscle of the hand as far as could be demonstrated clinically.

The physical signs resembled a thenar space infection of the palm, except that it was not painful and there were no systemic signs of an infective process. A needle was inserted into the lump, but only a few c.c. of fresh blood was withdrawn. A radiograph of the hand showed no involvement of the carpal or metacarpal bones, but a well-outlined soft-tissue swelling could be seen in the first interosseous space between the first and second metacarpal bones (*Fig.* 634). Chest radiography did not show a pulmonary lesion.

FIG. 634.—Radiographs of the right hand showing a soft-tissue swelling occupying the first interosseous space and extending into the palm. No involvement of the carpal or metacarpal bones is seen.

Exploration and biopsy were performed under general anæsthesia. A small incision was made over the palmar surface of the thenar eminence. A soft fleshy tumour was seen to be arising from beneath the flexor tendons; it was well encapsulated and appeared to be very vascular. There was no macroscopic evidence of any infiltration of the tumour to the surrounding thenar muscles. A small piece of tumour was taken for histological examination; the wound was closed. Histological section of the tissue removed showed that it was a rhabdomyosarcoma.

In spite of the rapid growth, the localized nature of the tumour suggested that it might be possible to perform a partial amputation of the hand. At operation it was soon evident, however, that there was an extension of the growth into the palm deep to the flexor tendons and that a conservative operation would not be possible. An amputation at the site of election in the forearm was therefore carried out.

THE SPECIMEN (*Figs.* 635, 636).—Dissection of the hand revealed a circumscribed, lobulated tumour measuring 7 × 6·5 × 4·5 cm. arising from the oblique head of the adductor pollicis muscle deep to the flexor tendons. The flexor sublimis and profundus with the first lumbrical were displaced forward over the tumour (*Fig.* 635). The growth extended down to the origin of the oblique head

on the capitate, the trapezoid, and the bases of the second and third metacarpal bones, and up to its insertion to the proximal phalanx of the thumb. The transverse head was not involved by the tumour, but was displaced upwards by the backward projection of the tumour between the first and second metacarpal bones.

Histological Description.—The biopsy specimen shows features identical with the tumour in the amputation specimen.

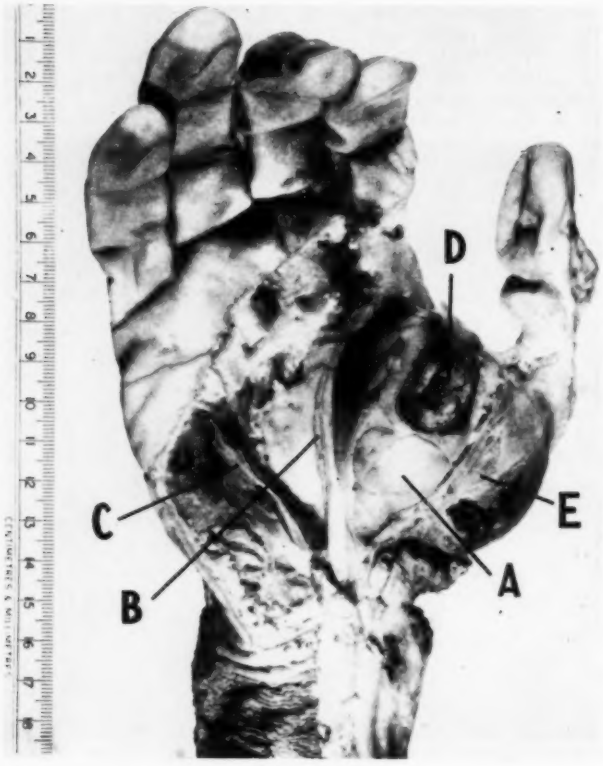


FIG. 635.

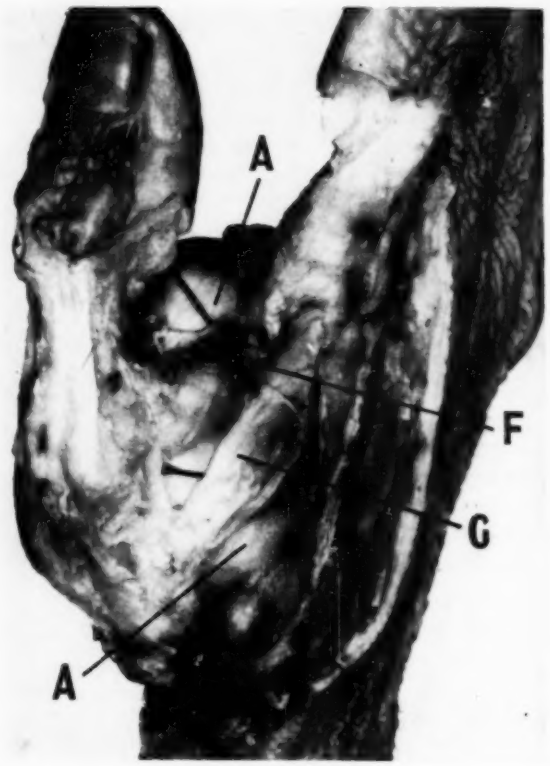


FIG. 636.

FIGS. 635, 636.—Dissection of the hand after amputation, showing the extent and relationship of the tumour. The flexor tendons, except those of the index finger, have been removed. A, The rhabdomyosarcoma involving the palm of the hand and arising from the adductor pollicis muscle. Extension backwards into the anatomical snuff-box can be seen in *Fig.* 635. B, Tendons of the flexor digitorum sublimis and profundus to the index finger and the first lumbrical muscle passing over the tumour. C, Fourth palmar interosseous. D, Area from which biopsy was taken. E, Thenar muscles. F, Transverse head of adductor pollicis muscle. G, First dorsal interosseous not involved in growth.

The neoplasm consists of closely packed intersecting bundles of eosinophilic fibres, separated by rather scanty collagen in which there are numerous poorly formed blood-vessels. The tumour cells, forming these elongated fibres, show a fairly regular appearance although the amount of eosinophilic cytoplasm varies a little and some cells show a prominent localized expansion of the fibre. The nuclei are plump, elongated structures showing a fine, open, chromatin net and usually one nucleolus. They appear to be typical muscle nuclei but are situated usually at the centre and only occasionally towards the side of the fibres. No sarcolemmal sheaths are seen. Longitudinal fibrils and cross-striations can be demonstrated in sections stained by hæmatoxylin and eosin. The transverse striations show all grades of differentiation, and have been confirmed by Mallory's phosphotungstic acid hæmatoxylin, by Heidenhain's iron hæmatoxylin, and by Holmes's stains. Mitoses are only moderately frequent and no multinucleate giant cells are found. At the periphery of the tumour there is some increase in the proportion of collagen, but this is infiltrated diffusely by neoplastic tissue as far as the edge of the specimen. Small arteries and nerves in this zone are completely surrounded by tumour, and some remains of normal voluntary muscle-fibres can be seen embedded in the sarcomatous tissue. (*Figs.* 637, 638.)

DISCUSSION

The comparative rarity of primary skeletal muscle tumours is indicated by the literature. Benenati (1903) made a list of the rhabdomyomatous tumours recorded from 1849 to 1900 and added a further case in which the tumour originated in an undescended testis. Only 9 of the 64 tumours which he listed arose in skeletal muscles. Küttner and Landois (1913) doubted whether many of the previously recorded cases were in fact rhabdomyosarcomas, but Stout (1946) accepted 107 cases of primary skeletal rhabdomyosarcomas from the previous literature and added 14 further cases.

In 1952 Pack and Eberhart added a further 100 cases of skeletal rhabdomyosarcomas treated at the Memorial Cancer Center in New York from 1929 to 1949. In spite of this rather large number of cases, however, these authors agreed that such tumours are very rare and they calculated that, on the basis of relative weights of tissue per pound of flesh, skeletal muscle has fewer tumours than any other tissue.

Many of the earlier descriptions of these neoplasms have left some doubt as to their muscular nature; the possibility of some normal or degenerate muscle-fibres being mistaken for neoplastic cells has not always been fully recognized. Moreover

some of the more malignant tumours show few, if any, immature cross-striated fibres, and this fact alone has caused much difference of opinion as to whether certain examples of the tumour should be included in the group. Rakow (1937), Pack and Eberhart (1952), Abrikossoff (1926, 1931), and Stout have all allowed, in their classifications, that cross-striations may not be demonstrable in some of the less differentiated tumours, and Jônsson (1938) went so far as to report 39 skeletal rhabdomyosarcomas, in none of which cross-striations could be observed.

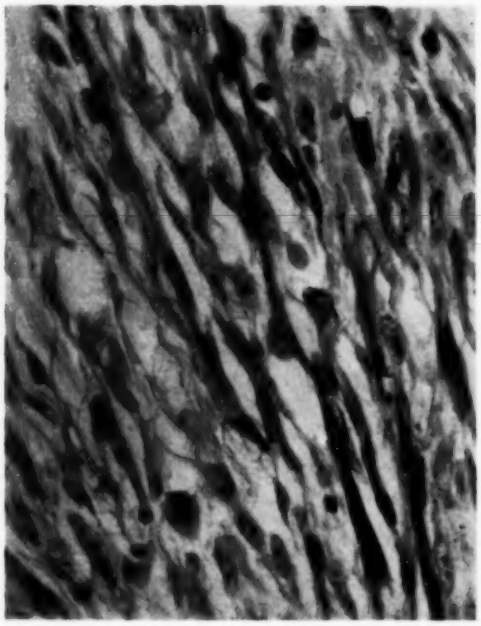


FIG. 637.—Shows the spindle-shape tumour cells, some of which contain poorly developed cross-striations. Heidenhain's iron hæmatoxylin stain. (× 400.)

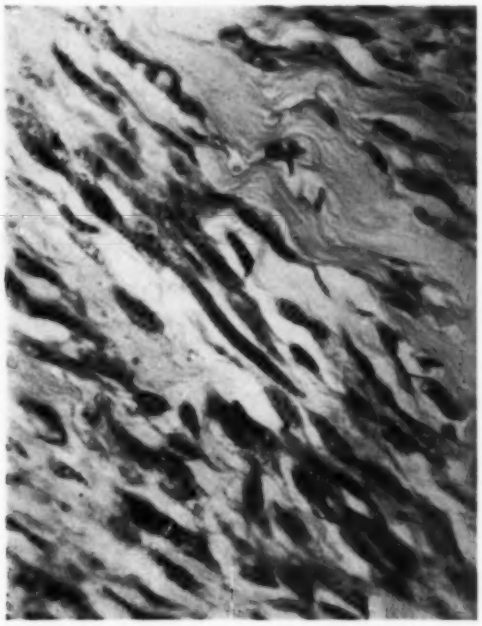


FIG. 638.—Shows one of the occasional well-differentiated muscle-fibres. Heidenhain's iron hæmatoxylin stain. (× 400.)

Most pathologists recognize many characteristic features shown by these growths—eosinophilic 'strap-like' cells containing prominent longitudinal fibres, bulging of these spindle cells, multinucleate giant cells, and the vacuoles, granules, and fibrils, which probably represent precursors of cross-striations and which have been described by Abrikossoff (1926, 1931), Wolbach (1928), Cappell and Montgomery (1937), and others. The majority, however, do not finally label such tumours as rhabdomyosarcomas until some definite cross-striations have been demonstrated.

The diagnosis therefore rests to some extent upon the skill and patience of the observers—some tumours will be missed and these tend to counterbalance those included on insufficient evidence.

Several articles stress the fact that many of these neoplasms show areas of myxosarcomatous appearance and it seems likely that many tumours diagnosed as fibrosarcomas or myxofibrosarcomas have been, in actual fact, of muscular origin. Greig (1917), for instance, recorded a myxosarcoma of the soft palate, the diagnosis of which was later doubted by Martin and Alexander (1924), who described a rhabdomyosarcoma occurring in the same region. Myxomatous areas were frequent in their tumour and the true nature of the case was only ascertained after careful study of certain fields in the surgical specimens. Cappell and Montgomery re-examined the tissue from Greig's case and were successful in proving that it was indeed another rhabdomyosarcoma.

There is some discrepancy of opinion in regard to the commonest age at which these tumours develop. Of Pack and Eberhart's cases 65 per cent were in the 40–70 year group and the mean of the 121 cases reviewed by Stout was 42·1 years. It must be remembered, however, that these authors have included tumours which might not satisfy the criteria of some pathologists, and it has been pointed out by Willis (1953) that many of the more recent and adequately illustrated papers have described such tumours as occurring in children or adolescents. Nevertheless, he admits that undoubted examples in adults do occur.

Rakow (1937) charted, anatomically, the sites of the tumours recorded by Montpellier (1929), MacCallum (1933), and himself. No example was recorded in the hands. Pack and Eberhart (1952), however, indicated that one of their 100 cases occurred in the hand and this is the only rhabdomyosarcoma at this site that we have discovered in the previous literature.

The rarity of primary skeletal neoplasms has been put down to the limited capacity of striated muscle to regenerate. Keith (1933) has been quoted as declaring that no new voluntary muscle-fibres are formed normally after birth, and it has been suggested that the occurrence of rhabdomyosarcomas in children and adolescents may be related to the possibility that very occasional muscle cells in early life may still retain the ability to proliferate and, on occasions, to form malignant new growths. Le Gros Clark (1946) and Cappell and Montgomery (1937) describe a modified type of regeneration of voluntary

muscle-fibres after injury, and the latter authors noted changes which bore some resemblance to the tumours described in their article. The possible influence of trauma in the aetiology of such tumours must therefore be considered.

The cases described by Buhl (1865) and by Muller (1917) are often quoted as examples of the association, but neither of the histories, in Buhl's two cases, is convincing. In the first, the patient noted some pain in the back, after falling downstairs eight years previously to the formation of a tumour in the spinal muscles. In the second it is merely stated that the tumour developed in the pectoralis major muscle after a ' strain '. Muller's patient, however, sustained fractures of the femur at the age of 4 years, and again at 11 years. He developed at the site of the fractures an inflammatory reaction which persisted until the age of 48 years, when the tumour developed at the same site. No cross-striations were demonstrated in this tumour.

Childs (1949), however, described an undoubted rhabdomyosarcoma which developed in the pectoral muscle of a woman aged 62 years. She had undergone a local mastectomy for a large cyst in the breast tissue, and two years later developed this neoplasm in the muscle immediately beneath the operation scar. Its origin in traumatized muscle was presumed.

Pack and Eberhart (1952) recorded that 7 per cent of their patients recalled previous trauma to the part but the authors dismissed this as insignificant. Stout found trauma mentioned in 11·5 per cent, a figure which he also regarded as hardly significant.

In our case there is a clear history of a crush injury, nine years previously, which caused disarticulation of the trapezoid, a fractured scaphoid, and median nerve palsy associated with marked atrophy of the thenar muscles. After prolonged physiotherapy over the course of two years the muscles recovered partially, and it was in one of these muscles which takes origin from the trapezoid bone that the tumour had subsequently developed, the transverse head of the muscle remaining uninvolved.

It is a well-known fact that many malignant tumours arise in tissues undergoing proliferation for some reason, and the regeneration of tissues following trauma has, both in human beings and experimental animals, been incriminated as a condition predisposing occasionally to neoplastic change.

It is generally impossible to assess the importance of injury in the aetiology of human malignant disease. Individual patients and surgeons are so apt either to disregard or over-emphasize such a history. In the present case it seems probable that there is a relationship. On the other hand, it must be admitted that the type of cellular proliferation which has been usually linked with the initiation of neoplasms does not seem to occur after injury to voluntary muscles.

Dissection of the tumour in our case shows that this is an apparently well-localized neoplasm, and study of the histological sections shows only moderately frequent mitoses and little cellular pleomorphism. Reference to the literature, however, indicates that rhabdomyosarcomas are typically well-circumscribed, lobulated tumours which, however, are renowned for their capacity to recur and to become progressively more malignant during each recurrence.

Apart from the surgical impracticability of removing many of these tumours locally, it seems that in most cases they behave as malignant neoplasms, in spite of their apparently circumscribed appearance. Gordon-Taylor (1940) stated in regard to these growths " . . . the abolition of the word encapsulation is better calculated to relegate the operation of so-called enucleation for these tumours into the background ". Stout maintained that all peripheral primary muscle tumours should be regarded as malignant.

In our case it was decided to amputate through the forearm for reasons previously noted and subsequent histological examination of the tumour revealed no real fibrous encapsulation, but progressive cellular neoplastic proliferation at the periphery.

Finally, we should like to emphasize the confusion which may exist clinically between malignant connective-tissue tumours in this region and acute or subacute inflammatory conditions. Simenstad (1930), for instance, recorded a spindle-cell sarcoma in the small muscles of the hand which was treated for two years as an inflammatory lesion before its true neoplastic nature was appreciated, and Kleinberg (1948) described a myxofibrosarcoma of the hand which simulated at first an infection of the mid-palmar space. In our case there were some signs suggestive of a thenar space infection, but there was no pain and needling of the swelling did not produce pus.

SUMMARY

A rapidly growing malignant tumour has been described. It arose in the oblique head of the adductor pollicis muscle of a man aged 33 years, after a severe crush injury of the hand sustained nine years previously. Many immature muscle-fibres containing cross-striations have been demonstrated, establishing that the tumour is a rhabdomyosarcoma. Its comparative rarity and the relationship to injury are discussed.

We should like to thank Professor Sir James Paterson Ross for his advice and permission to publish this case ; Mr. J. W. Miller for preparation of the histological material ; Mr. P. R. Crocker for the photomicrographs ; and the photographic department of St. Bartholomew's Hospital for photographs of the specimen.

REFERENCES

ABRIKOSSOFF, A. I. (1926), *Virchows Arch.*, **260**, 215.
— — (1931), *Ibid.*, **280**, 723.
BENENATI, V. (1903), *Ibid.*, **171**, 418.
BUHL (1865), *Z. Biol.*, **1**, 263.
CAPPELL, D. F., and MONTGOMERY, G. L. (1937), *J. Path. Bact.*, **44**, 517.
CHILDS, P. (1949), *Brit. J. Surg.*, **37**, 230.
CLARK, W. E. LE GROS (1946), *J. Anat., Lond.*, **80**, 24.
GORDON-TAYLOR, G. (1940), *Brit. J. Surg.*, **28**, 1.
GREIG, D. M. (1917), *Edinb. med. J.*, N.S. **19**, 24.
JÔNSSON, G. (1938), *Acta radiol., Stockh.*, Suppl. **36**, 1.
KEITH, Sir A. (1933), *Human Embryology and Morphology*. London : Arnold.
KLEINBERG, S. (1948), *Bull. Hosp. Jt. Dis.*, **9**, 81.
KÜTTNER, H., and LANDOIS, F. (1913), *Dtsch. Z. Chir.*, **25**, 1.

MacCallum, P. (1933), *Aust. N.Z. J. Surg.*, **2**, 296.
Martin, G. E., and Alexander, W. A. (1924), *J. Laryng.*, **39**, 312.
Montpellier, J. (1929), *Bull. Ass. franç. Cancer*, **18**, 539.
Muller, H. R. (1917), *J. Cancer Res.*, **2**, 393.
Pack, G. T., and Eberhart, W. F. (1952), *Surgery*, **32**, 1023.
Rakow, A. I. (1937), *Amer. J. Cancer*, **30**, 455.
Simenstad, L. O. (1930), *Int. J. Med.*, **43**, 431.
Stout, A. P. (1946), *Ann. Surg.*, **123**, 447.
Willis, R. A. (1953), *Pathology of Tumours*, 2nd ed. London: Butterworth.
Wolbach, S. B. (1928), *Arch. Path. (Lab. Med.)*, **5**, 775.

SPONTANEOUS RUPTURE OF THE STOMACH

By T. McW. MILLAR, JOHN BRUCE, and J. R. S. PATERSON, Edinburgh

Spontaneous rupture of the stomach is an unusual and highly lethal event. In this communication we are reporting two fatal cases, one of which was complicated by air embolism, itself an equally rare phenomenon.

CASE REPORTS

Case 1.—The patient was an elderly woman, 71 years of age. Her admission to hospital was consequent upon a moderate hæmatemesis three days before; but she had a long history of dyspepsia which she had controlled, more or less with success, by various antacid powders. There had been one previous episode of bleeding; but in the months before admission she had been aware of a deterioration in appetite and in general health; indigestion had also become more persistent and more incapacitating.

She was a well-preserved old lady, moderately hypertensive, but otherwise in good physical condition. The clinical suspicion of a gastric lesion was confirmed, and radiological examination showed a large gastric ulcer in the pyloric antrum, with marked narrowing in the prepyloric region and a considerable gastric residue.

Our radiologist colleague was convinced that there was also prolapse of the duodenal mucosa through the pylorus, with a typical indentation deformity of the duodenal cap.

Gastroscopy was unhelpful, but by reason of her age and lack of spinal mobility, the examination was less adequate than usual. Nocturnal aspiration of the night secretion of the stomach produced a very moderate volume of gastric juice which contained no free acid.

Operation was advised because of the size of the ulcer, the suspicion of malignancy, and the gastric retention. This advice was summarily rejected, and the old lady was determined to leave hospital.

At 4 p.m. on the day of her death, she complained of slight epigastric discomfort which caused her to refuse afternoon tea, but at 6 p.m. she ate some milk pudding. At 7.45 p.m. she was seized with violent abdominal pain. This was so severe as to cause her to cry out; she likened it to being " full of wind which she could not bring up ", and the nursing staff reported that she had been breathing heavily, taking great gulps of air.

Clinical examination shortly afterwards suggested perforation of her gastric ulcer. She was pale, cold, and clammy, as she lay moaning in bed; and her systolic blood-pressure reading was 100 mm. Hg—a considerable fall in view of her previous hypertension.

The abdomen was distended, and quite boarded. Save for a few faint sounds in its right lower quadrant the abdomen was silent; and even the few initial sounds ceased after the passage of a small stool.

Operation was deemed necessary on the strength of a diagnosis of perforated peptic ulcer. Meanwhile, morphine was administered, and she was prepared for operation.

An attempt to pass a duodenal tube failed. There was temporary improvement in her condition, reflected in a blood-pressure recording of 138/85; but on transfer to the anæsthetic room she again became very collapsed. The limbs were again cold, and presented an unusual mottled or marble-like appearance; there was profound hypotension, and the peripheral pulses were impalpable. The abdomen was more noticeably distended, and crepitations were detected in the abdominal and thoracic walls, and in the left side of the neck.

A diagnosis of tension pneumoperitoneum was suspected, and with a blood transfusion in progress, a small paramedian incision was made in the upper abdomen. There was only a small escape of gas, in place of the large amount expected; and in addition, about two pints of watery greenish fluid poured out.

The stomach was grossly enlarged but collapsed. On investigation, a large tear was discovered at the middle of the lesser curvature; all coats of the stomach were equally involved, and the small omentum was separated over the distance of the rent. An even more strange appearance was presented by the subserous vessels of the stomach. The contents of the vessels consisted of a series of thin disks of blood widely separated by bubbles of air, and the entire stomach wall was crepitant.

Her condition had by now gravely deteriorated, and death occurred at 9.45 p.m., some two hours after the start of the episode.

Autopsy Findings.—At post-mortem examination all the vessels examined contained a considerable quantity of air, and the heart could be floated in water. The subcutaneous emphysema detected clinically in the abdominal wall and in the neck was due to air in the tissues also. A careful search was made for a site of air entry into the circulation, but without success.

The Stomach.—The stomach was very large. Rupture had occurred, not at the site of peptic ulceration but at the middle of the lesser curve. The rent was a ragged one, approximately 8 cm. long, with edges thin and necrotic.

There was no apparent obstruction in the cardio-œsophageal area; but the pylorus was largely occluded by redundant mucosa, and failed to admit the tip of a finger.

Comment.—Presumably the gross spontaneous rupture of the stomach was precipitated by spasm, with total occlusion of the pyloric outlet. The most remarkable feature, however, was the fact that it was not the ulcerated area which yielded, but apparently healthy stomach proximal to it.

A short time after the above experience we encountered a second case of spontaneous rupture of the stomach. Though in some ways comparable, certain important differences were noted that may shed some light on the nature of the accident.

Case 2.—This patient was an elderly woman, 71 years of age, who was admitted as an emergency because of acute abdominal pain. For some weeks she had complained of discomfort in the upper abdomen, for which she had been taking baking soda. Three hours prior to

admission she was seized by very severe central epigastric pain which remained more or less constant, and rapidly resulted in her complete prostration. There had also been some nausea, and small amounts of clear fluid were vomited.

Twelve months previously a carcinoma of the transverse colon had been resected ; there was then no evidence

FIG. 639.—*Case* 2. The stomach, showing the area of rupture on the anterior wall.

of distant metastases, and when last seen six months prior to admission, she was apparently well.

On admission the woman was obviously very ill, presenting the classical picture of severe peripheral circulatory failure. The systolic blood-pressure was 90–100 mm. Hg, but the diastolic pressure could not be determined accurately. The abdomen was grossly distended and tympanitic, and the abdominal parietes were extremely tense and tender. Bowel-sounds could not be detected.

An intravenous infusion was started, and an attempt was made to pass a Levine's tube. This was unsuccessful, neither gas nor liquid being aspirated ; and the patient died some fifty minutes after admission.

Immediately after death crepitant swelling of the eyelids developed with dramatic rapidity ; later this spread into the neck, and on to the chest wall, and subcutaneous emphysema became very marked within thirty minutes of death.

AUTOPSY FINDINGS.—At autopsy the distension of the abdomen was found to be due partly to the presence of free gas under tension in the peritoneal cavity and partly to gross distension of the stomach. There was no exudate on the surface of the stomach or the other viscera, and only a small amount of blood-stained fluid in the peritoneal cavity. The presence of subcutaneous emphysema in the abdominal wall, chest wall, and neck was confirmed.

The Stomach.—The stomach was pear-shaped and was the size of a full-term uterus. On the anterior wall near the lesser curvature and immediately below the gastro-œsophageal junction, there was an area nearly 6 cm. in diameter where the peritoneum and underlying stomach wall were dark brown in colour (*Fig.* 639). The peritoneum was everywhere intact, but bubbles of gas were present between the layers of the gastro-hepatic omentum, and the gas could be traced upwards through the œsophageal hiatus. When the stomach was opened, the discoloured area was seen to be due to an irregular tear in the mucosa and muscle of the lesser curvature, the tissues in the region of the tear being soft and brown. Immediately behind this lesion there was a similar but smaller patch involving mucosa only. The rest of the gastric wall was very thin.

The pyloric opening was extremely small, and would not admit a finger. A small diverticulum was present in the duodenal wall immediately distal to the pylorus, but there was no great thickening or distortion of the first part of the duodenum.

The distension of the stomach was due largely to gas, there being only a moderate amount of turbid fluid content. The remainder of the abdominal viscera were normal and there was no evidence of recurrence of the colon tumour. The line of the colon anastomosis was barely detectable.

The heart was not enlarged, and there was no evidence of air in the ventricles, coronary vessels, or pericardium.

The right pleural sac contained foul-smelling gas under tension, which had produced complete collapse of the right lung. The left pleural cavity did not contain gas, but the lung was collapsed as a sequel to gross elevation of the diaphragm on that side. The fat in the mediastinum contained bubbles of gas, and gas was also present in the muscles of the chest wall.

Comment.—In this case the mucous and muscular layers of the stomach wall had ruptured, allowing the escape of contents between the intact peritoneal layers of the lesser omentum, and upwards into the peri-œsophageal tissues ; in the earlier case, the peritoneum had been torn also, so that the gastric contents were discharged into the peritoneal cavity.

Each case represents a variety of spontaneous rupture, therefore ; the first a complete spontaneous rupture of all coats, the second an extra-peritoneal, or intra-omental rupture.

DISCUSSION

Rupture of the stomach is a rare accident, and particularly so in the absence of trauma. The mobility of the stomach, its flaccid walls, its relatively protected situation, and the presence of safety vents at the pyloric and gastro-œsophageal openings ensure its safety unless it is grossly overdistended. In most of the cases of traumatic rupture, the viscus has in fact been distended with food or with fluid, and it has been supposed that spasm of the pylorus or of the cardia, or of both, complete the ' setting ' in which the stomach literally bursts.

Rupture in the absence of trauma—so-called *spontaneous rupture*—though still more uncommon, has been recognized for a long time. In the early part of the last century it was regarded as not infrequent ; but there is no doubt that the large majority of these early cases were in fact perforations of a peptic ulcer, a lesion not defined until Cruveillier described it, and some of its consequences, in 1829. The earliest proved example of true spontaneous rupture that we have been able to trace was reported to the Liverpool Pathological Society during the Session 1845–46 by James Carson, whose statue now

stands in the hall of the Liverpool Medical Institution. The case is recorded at length in the Society's *Transactions* which were published in the *Edinburgh Medical Journal* of 1846. Like the proceedings of other comparable Societies of that time, these *Transactions* are remarkable both for catholicity of substance and for elegance of presentation.

Carson's case is of some historical interest, and deserves notice, because he records the observation of a sign that was also present in both the present cases, viz. subcutaneous emphysema. The patient was a sailor of 20 years, who experienced severe transient epigastric discomfort following his mid-day dinner. After a generous evening meal, he was seized with violent abdominal pain ; and on admission to hospital he had a tympanitic abdomen and all the signs of shock. In the succeeding few hours, despite warm water and turpentine enemata, draughts of both asafœtida and cinnamon, and bleeding, his belly became more distended and resonant, and his general condition worsened. Just before death at 8 p.m. extensive crepitation was noted in the neck, upper part of the chest, and in the abdominal wall.

At autopsy the stomach was found to have undergone volvulus, with rotation of the greater curvature upwards and to the right side on the axis of the lesser curvature. The rupture was situated in the region of the greater curvature. Carson attributed the absence of vomiting to the volvulus, though he did not blame this for the subsequent rupture.

Since Carson's account a number of other cases have been reported. In most of them attention is drawn to the presence of extreme gastric distension, from overeating or drinking to excess ; and more than once sodium bicarbonate had been taken immediately before the catastrophe in an attempt to relieve epigastric discomfort.

That obstruction at the stomach orifices is also a potent, and may be an essential, factor is supported by the frequent reference in these reports to pyloric obstruction—by carcinoma, congenital duodenal obstruction, incarceration in a diaphragmatic hernia, valvular duodenal stenosis, and, as in Carson's case, complete gastric volvulus.

It might be supposed that overdistension of the distally obstructed stomach could be relieved by vomiting ; but the literature is silent about the state of the cardiac orifice save for Carson's reference to volvulus, which provides an obvious and understandable explanation. The mechanisms preventing regurgitation from stomach to œsophagus are not well understood, but certain facts are clearly established. Thus the ' slight curve ' by which in anatomical literature the œsophagus is supposed to merge into the lesser curvature of the stomach is, in fact, almost a right-angled junction, the angulation of which is maintained by the encircling fibres of the right crus of the diaphragm (*Fig.* 640). To these crural fibres some have assigned a sphincteric role which is brought into play during inspiration ; others believe that the cardio-œsophageal orifice is a valve, depending for its efficiency on the angle between the œsophagus and the fundus of the stomach. It may be that in gross overdistension the valvular mechanism is only too effective ; and with repeated aerophagy in an attempt to bring up wind, the valve may be forced in one direction and immediately closed in the reverse. Apart from the swallowing of additional air, once gastric distension has reached a dangerous level the secretions of the stomach, and possibly gaseous transfer across the walls of engorged capillaries, will gradually distend the stomach to the point of bursting.

FIG. 640.—Longitudinal section of thorax and abdomen. The terminal part of the œsophagus appears in transverse section, indicating that its course is entirely horizontal.

There have been a number of experimental studies of the resistance of the healthy stomach to increasing distension. Revilloid (1885) had to exceed 4 litres before he was able to demonstrate rupture of the cadaver stomach, and largely comparable experiences have been reported by other observers.

The Site of Rupture.—In the majority of recorded instances the tear has been on the lesser curvature, as in the present cases. It has been postulated (Fraenkel, 1906) that absence of mucosal folds on the Magenstrasse reduces the coefficient of elasticity of the gastric wall. Furthermore, Key-Aberg (1891) found that the distended stomach tends to become spherical, so that the fixed lesser curvature is called upon to withstand an amount of stretching which is relatively greater than that of the rest of the viscus.

Certainly the edges of the aperture are usually thin, necrotic, and ragged, and on microscopical examination there is often submucosal hæmorrhage or infarction. The process of rupture begins with tearing of the mucosa, and it has been suggested that this is preceded by ischæmic necrosis brought about by the overdistension.

The experiments of Talma (1890) suggest that this may be so. In distension studies on the rabbit stomach he was able to cause softening of the mucous

membrane and frank ulceration, as well as areas of infarction due to venous occlusion. The possible relationship of less serious distension to the acute erosions sometimes found at operation for massive gastroduodenal hæmorrhage is a fascinating conjecture, though without relevance to the present occasion.

The pathological features of the rupture in our second case are in keeping with the experimental observations. Here there was evidence of necrosis both of the mucous and the muscle layers; and though gas had escaped between the layers of the small omentum, the stomach was still grossly distended, and if death had not occurred a complete tear might well have been established.

It is possible that in the earlier case the complete tear was preceded by phases of mucosal and muscular rupture, though evidence of this was not recognized. The appearance of cervical and mediastinal emphysema suggests, however, that there had been an extensive discharge of gas into the extraperitoneal tissues.

Clinical Features.—The clinical picture is essentially one of an intra-abdominal catastrophe associated with severe shock, and usually or eventually subcutaneous emphysema.

The Subcutaneous Emphysema.—This appears to be a characteristic clinical finding. It was a noticeable feature in Carson's original report (1846), and it was present in both our patients. Carson first detected the crepitations in the root of the neck, as in our second case; and this suggests that the gas may pass extraperitoneally to the mediastinum and so to the cervical region, as well as to the flanks and to the thoracic wall, where it was particularly noticeable in our first patient. It is interesting to note that crepitant emphysema of the neck occurs also in spontaneous rupture of the œsophagus (Mackler, 1952).

We suggest that, following the onset of severe upper abdominal pain, the combination of: (1) Tympanitic abdominal distension; (2) Rigidity of the abdominal parieties; (3) Subcutaneous emphysema; and (4) Evidences of shock, constitute a diagnostic tetrad that may serve to distinguish rupture of the stomach from other major abdominal or pseudo-abdominal shock-producing lesions such as pancreatitis, coronary thrombosis, or intestinal infarction.

The Cause of Death.—Few patients have survived gastric rupture. This is difficult to understand, considering the clinical behaviour of perforated peptic ulcer. It is tempting to believe that the sudden release of pressure within the distended stomach evokes a grave reflex vascular derangement. In one of our cases we believe that death was hastened by concomitant air embolism, but this appears to be a hitherto unrecorded complication.

The Air Embolism.—The site of air entry in this case is a matter for surmise. Presumably it occurred through torn gastric veins in the vicinity of the gastric rupture; if so, the gas must have transversed the liver sinusoids to reach the systemic circulation. The curious marble-like appearance of the skin was very striking. It has been reported in other cases of air embolism (Martland, 1945; Hamby and Terry, 1952).

The appearances both at operation and at autopsy suggested that the quantity of intravascular gas was considerable, and this probably explains the rapidly fatal outcome. Nevertheless, there is no certain knowledge of the amount of air needed to produce fatal embolism. This must obviously depend on many factors—age and cardiovascular status, and the rate and site of air aspiration in addition to quantity (Richardson, Coles, and Hall, 1937). It has been computed that some hundreds of cubic centimetres must gain access in the case of systemic embolism, but that in the case of the pulmonary veins the amount is very considerably less, and may be even as little as a few cubic centimetres. The enhanced danger of the latter is in consequence of the liability to cerebral and coronary occlusion; whereas in embolism of the systemic veins death usually results from cardiac failure, since the frothy blood which accumulates in the right ventricle is simply compressed, rather than propelled onwards by the contractions of the ventricular muscle.

In our case the terminal events were so rapid that it was impossible accurately to attribute the fatal outcome to either a pulmonary or a cardiac mechanism, nor was there an opportunity of attempting to influence the embolism by postural and other methods.

SUMMARY

1. Two cases of spontaneous rupture of the stomach are reported.

2. In one of these, air embolism was responsible for very rapid death.

3. It is suggested that tympanitic distension of the abdomen, shock, and subcutaneous emphysema following quickly on sudden severe epigastric pain is a diagnostic triad which will serve to exclude such conditions as acute pancreatitis, coronary occlusion, and intestinal infarction.

BIBLIOGRAPHY

CANNON, P. R., and HALBERT, B. (1929), *Arch. Path.* (*Lab. Med.*), **8**, 611.
CARSON, J. (1846), *Edinb. med.-surg. J.*, **66**, 28.
CAVAILLON and LERICHER (1908), *Lyon méd.*, **111**, 84.
FRAENKEL, R. (1906), *Z. klin. Med.*, **89**, 113.
GLASSMAN, D. (1929), *Ann. Surg.*, **89**, 247.
HAMBY, W. B., and TERRY, B. N. (1952), *Surgery*, **31**, 212.
HERZOG, E. (1928), *Zbl. allg. Path. path. Anat.*, **41**, 437.
KEY-ABERG, A. (1891), quoted by GLASSMAN, D. (1929).
LADKIN, R. G., and DAVIES, J. N. P. (1948), *Brit. med. J.*, **1**, 644.
LEMMON, W., and PASCHAL, G. W. (1941), *Ann. Surg.*, **114**, 997.
MACKLER, S. B. (1952), *Surg. Gynec. Obstet.*, **95**, 345.
MARTLAND, H. S. (1945), *Amer. J. Surg.*, **68**, 281.
MOUCHET, P. (1946), *Paris méd.*, **2**, 323.
MURDFIELD, P. (1926), *Klin. Wschr.*, **5**, 1613.
PLATT, W. R. (1945), *Arch. Path.* (*Lab. Med.*), **40**, 403.
REVILLOID, E. (1885), *Rev. méd. Suisse rom.*, **1**, 193.
RICHARDSON, H. F., COLES, B. C., and HALL, G. E. (1937), *Canad. med. Ass. J.*, **36**, 584.
SEEGER, S. J. (1930), *Amer. J. Dis. Child.*, **40**, 334.
TALMA, S. (1890), *Z. klin. Med.*, **17**, 10.

GIANT RUGAL HYPERTROPHY OF THE STOMACH

By H. DAINTREE JOHNSON and ALFRED STANSFELD
FROM THE DEPARTMENTS OF SURGERY AND PATHOLOGY, ROYAL FREE HOSPITAL

GIANT rugal hypertrophy of the stomach was first clearly described by Menetrier (1888). He called it 'polyadenome en nappe', and distinguished it from 'polyadenome polypeux' (multiple polyposis), which he described in the same paper. Recently Kenney, Dockerty, and Waugh (1954) surveyed the literature and culled from it 47 published cases of giant rugal hypertrophy. They added a further 19 from the records of the Mayo Clinic.

CASE REPORT

The patient, a male photo-engraving operator aged 48 years, presented as a case of anæmia, for which he was referred to our colleague, Dr. Una Ledingham. He complained only of tiredness and breathlessness on exertion. However, on questioning he admitted to a tendency to mild indigestion "all his life", associated with flatulence, and recently with slight dysphagia. The dyspeptic symptoms had always responded to alkalis. There had never been vomiting or, to the best of his knowledge, any melæna. Except for the evident anæmia, physical examination was essentially negative.

Investigation revealed a hæmoglobin level of 8·0 g. per 100 c.c. (54 per cent), with a colour index of 0·87 and packed-cell volume of 27 per cent. A bone-marrow specimen showed moderate normoblastic hyperplasia, and a histamine test elicited a normal acid response. The barium meal radiograph (*Fig.* 641) was reported as showing "an odd, irregular filling defect on the lesser curve of the stomach just below the cardia, not typical of new growth and possibly due to swollen mucosa".

After a repeat, a second report read: "Re-examination confirms the presence of a fairly large irregularity on the upper end of the lesser curve. The mucosa in the area appears partially destroyed and 'finger print' defects are present. Spot films show an ulcer which lies within the gastric outline. The findings are very suggestive of a neoplasm."

Wassermann and Kahn reactions were negative and the erythrocyte sedimentation rate was 7 mm. in one hour. After transfusion, when the hæmoglobin level had reached 12 g. per 100 c.c. (84 per cent) the blood-urea was 58 mg. and serum-chlorides 520 mg. per 100 c.c. Serum-sodium and -potassium were normal. Unfortunately the plasma-proteins were not estimated (in some of the previous cases in which such estimations were made there was found to be hypoproteinæmia).

AT OPERATION.—On a diagnosis of gastric neoplasm, surgical exploration was undertaken. Outside the stomach no abnormality was detected. The stomach itself was moderately enlarged and was felt to contain a soft, sausage-shaped swelling attached to the lesser curvature, and seeming to extend from the cardia to within 2–3 in. of the pylorus, tapering off at either end. Though its limits were easy to feel in a transverse direction, its upper and lower limits were indefinable through the stomach wall, a feature which in retrospect we believe to be important in diagnosis at laparotomy.

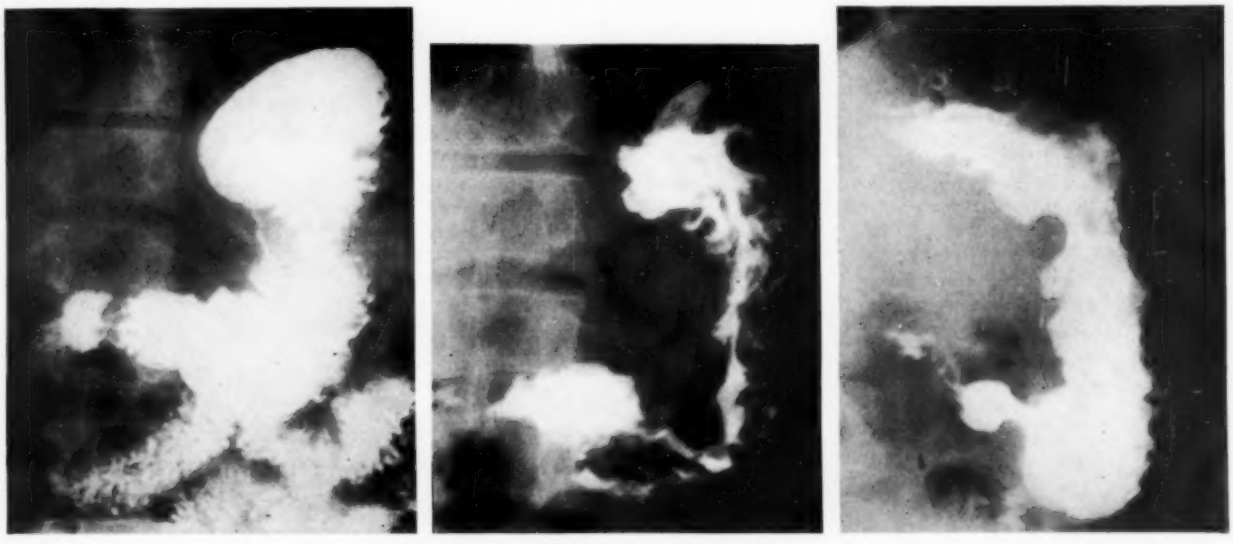


FIG. 641.—Barium meal radiographs.

The lesion was judged to be a sarcoma and upper partial gastrectomy was decided upon. The resection extended from a point on the œsophagus 1 in. above the cardia down to the gastric antrum, 2 in. proximal to the pylorus.

The resected piece of stomach, on being opened, was found to contain three enormously hypertrophied rugæ lying one along and one on either side of the lesser curvature. At the upper end, a fold the thickness of a little finger encircled the cardiac orifice and was more or less continuous with the giant folds on the lesser curvature, each of which reached a breadth of more than an inch for most of its length. Below the cardia, in the anterior of the three giant rugæ, were one small and two larger ulcers of moderate depth containing blood-clot. They did not have features suggesting any great chronicity.

At the pyloric end where the rugæ tapered off it was found that the resection had not included the whole length of the abnormal folds, for some degree of pathological hypertrophy could be seen to continue right down to the pylorus. However, after the specimen had been transected and examined the diagnosis of sarcoma was abandoned and therefore no further tissue was resected.

This may have been ill-advised for the hypertrophied mucous membrane, on account both of its bulk and of its friability, greatly embarrassed the performance of anastomosis with the œsophagus.

After operation the patient made normal progress for five days. On the sixth day he collapsed, and it was evident that his anastomosis was leaking. Oral feeds

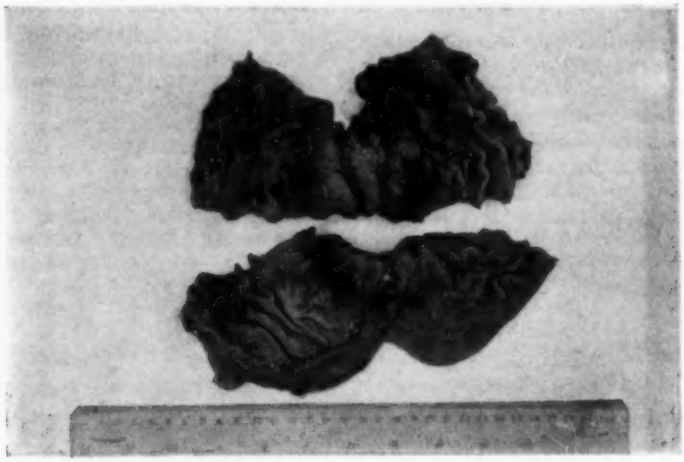


FIG. 642.—View of opened and transected stomach after removal of mucus.

were stopped, a drain was inserted under local anæsthesia and resuscitative measures instituted, but there was little response and he succumbed less than 24 hours afterwards. At post-mortem examination purulent peritonitis was present, due to leakage of the gastro-œsophageal anastomosis. No other significant pathological changes were found.

Pathological Description.—The operation specimen consisted of the proximal four-fifths or so of the stomach. Running along the whole length of the lesser curve there

FIG. 643.—Cross section of opened stomach showing giant rugæ on the lesser curve.

were three wide ridges of mucosa covered by quantities of mucus. On the summit of the anterior ridge there were three irregular hæmorrhagic ulcers. In addition to the main ridges on the lesser curve, several rugæ on the anterior and posterior walls of the stomach were swollen to a lesser extent. When the mucus had been removed, the surface of the abnormal rugæ was seen to be irregularly and finely corrugated, in marked contrast to the smoothness of the adjacent normal mucosa (*Fig.* 642). There was, however, no induration and the affected mucosa was freely mobile. On section the abnormal mucosa was seen to be greatly thickened and minute cysts could be made out in its deeper part with the naked eye (*Fig.* 643). The submucosa was œdematous and hæmorrhagic beneath the giant rugæ. The muscularis and serosa presented no gross abnormality.

Histology.—The mucosa at a distance from the giant rugæ was quite normal, whereas the mucosal pattern in the giant rugæ themselves was far from typical. In the intermediate areas different grades of disorder could be traced. The earliest detectable change consisted of a simple hypertrophy of the mucous membrane. The gastric glands were elongated and sometimes tortuous, but were lined throughout by cells of normal type—surface epithelium, chief cells, and parietal cells.

Where the hypertrophy was marked there was evident hyperplasia with piling up of the lining cells, particularly the surface-type epithelium of the gastric pits and gland necks, and the chief cells towards the bottom of the gland crypts. Between the hyperplastic but otherwise normal glands there occurred at intervals gland crypts which were lined throughout by mucus-secreting surface-type epithelium and, in the depths of the mucosa, some of these crypts were ballooned into mucus retention cysts (*Fig.* 644). In the neighbourhood of the giant rugæ the number of these abnormal gland crypts increased and some were

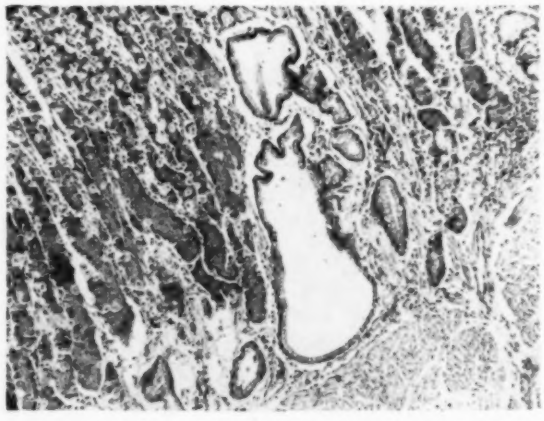


FIG. 644.—Base of hypertrophied mucosa showing gland crypts lined throughout by mucus-secreting epithelium. One crypt is greatly dilated. (× 120.)

lined by hyperplastic columnar epithelium which had lost the mucus-secreting property. On the giant rugæ themselves, the depth of the mucosa was further increased by folding of this layer, with the result that groups of dilated gland crypts, lined by mucus-secreting surface-type epithelium, were displaced downwards and mingled with the smooth muscle-bundles of the hypertrophic muscularis mucosæ, simulating malignant infiltration (*Figs.* 645–647). From the muscularis mucosæ groups of smooth muscle-fibres radiated upwards towards the surface between the mucosal glands, which were here separated by œdema (*Fig.* 648).

Some inflammatory-cell infiltration was present, but this was patchy and was clearly secondary to the mucus retention and other changes described. It should be stressed that the mucus-secreting epithelium lining many of the gland crypts was of the same type as the normal

gastric surface epithelium and no goblet cells of intestinal type were found; there was, in fact, no evidence of the 'intestinal metaplasia' characteristic of chronic gastritis. One of the ulcers showed on section a simple loss of surface with profuse hæmorrhage into the underlying tissues; the appearances were not those of a chronic peptic ulcer.

FIG. 645.—Section across the whole width of a giant ruga showing folding of the hypertrophied mucosa and downward displacement of cystically dilated gland crypts. (× 3.)

Apart from œdema and fresh hæmorrhage the submucosa showed no significant abnormality. It was observed, however, that large, dilated vessels, both veins and arteries, were present beneath the giant rugæ. The muscularis and serosa showed no alteration.

DISCUSSION

It was recognized by Menetrier (1888) that giant hypertrophy could affect either the whole or only a part of the gastric lining, but in reported cases the greater curvature of the stomach always seemed to have shown the severest degree of involvement. Thus a predilection for the greater curvature was found in 19 of the 20 cases reported by Kenney and others (1954). Our case is remarkable in that the abnormality was almost confined to the longitudinal rugæ of the lesser curvature. Apart from this unusual distribution, however, the pathological features are clearly those of Menetrier's 'polyadenome en nappe'.

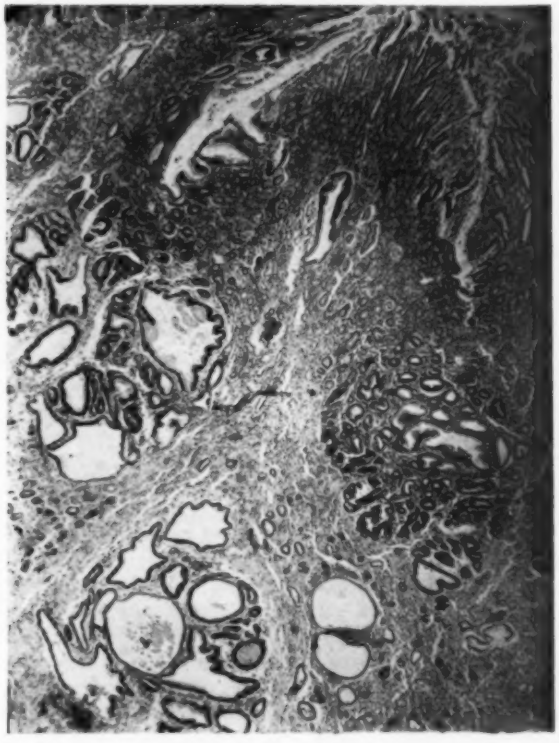


FIG. 646.—Distortion of the normal mucosal pattern on the summit of a giant ruga, simulating adenocarcinomatous infiltration. (× 24.)

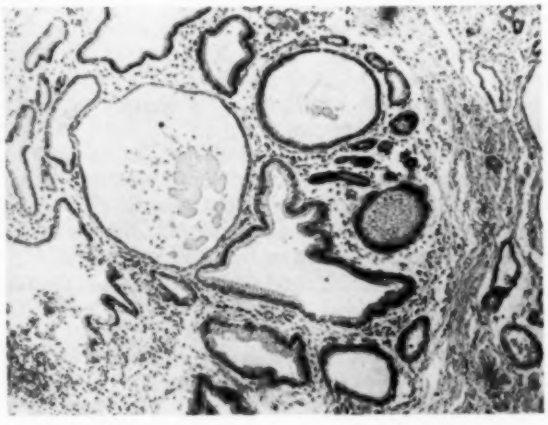


FIG. 647.—Higher power view of a group of cystically dilated glands seen in the bottom left-hand corner of *Fig.* 646. The gland crypts are intermingled with the fibres of the muscularis mucosæ, but their lining epithelium has an innocent appearance. (× 120.)

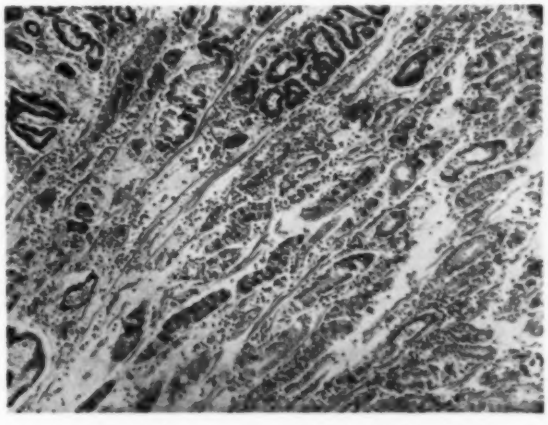


FIG. 648.—Mid-part of mucosa from summit of giant ruga showing numerous smooth muscle-fibres in œdematous interstitial tissue between hyperplastic gastric glands. There is marked inflammatory-cell infiltration in this region. (× 120.)

In spite of much speculation, the aetiology of this rare disorder remains obscure. Several authors since Menetrier have postulated an inflammatory origin for the disease, but have failed to explain its rarity in spite of the very high incidence of other forms of gastritis. Several facts militate against the

inflammation hypothesis, of which two may be cited: (1) the gastric acidity is often within normal limits (a point of distinction from Menetrier's 'polyadenome polypeux', where achlorhydria is the rule); and (2) the absence of histological evidence of inflammation in our case (and others) from all but the most severely affected parts of the mucosa—a fact which strongly suggests that such inflammatory changes as are present are of secondary importance.

If inflammation be excluded as a cause of 'polyadenome en nappe' then the use of the term 'gastritis' should be avoided in this connexion, since it is only likely to lead to confusion with so-called 'hypertrophic gastritis'; indeed this confusion is evident in some earlier publications. The essential features of the disease are clearly brought out in the name 'giant rugal hypertrophy of the stomach', which is both apt and unambiguous, the use of the term 'hypertrophy' underlining the growth disorder which is the central feature of the condition.

There is no recorded evidence of a hereditary predisposition to this disease and the age incidence, maximal in the fifth and sixth decades, makes it unlikely that the malformation is congenital. In most of the affected individuals no associated abnormalities have been found, but in the Mayo Clinic series 3 out of the 20 cases also had 'multiple endocrine tumours'.* These three cases were all severe, and the association suggests the possibility of a growth disturbance under endocrine control. Other authors have put forward the suggestion of a chemical stimulus, and a history of alcoholism has been reported once or twice. It appears that there is no constant occupational history, but our patient had handled a variety of chemicals, including potassium cyanide, nitric acid, and copper sulphate, in his work.

Other authors besides ourselves have drawn attention to the presence of large submucosal blood-vessels beneath the giant rugæ, but there was nothing in our case to suggest that the overgrowth was secondary to a vascular malformation. The development of localized rugal hypertrophy has been reported as a sequel to operations on the stomach, but we have not learned of any evidence suggesting that the pathology of these cases is the same as that of Menetrier's 'polyadenome en nappe'. It seems possible that a localized vascular disturbance with œdema may be the cause of the post-operative rugal enlargement.

Whatever the cause of giant rugal hypertrophy may be, it seems that the condition rarely undergoes malignant transformation. Matzner, Raab, and Spear (1951) cite a case of diffuse gastric carcinoma, supposedly preceded by giant rugal hypertrophy, though the earlier presence of this condition was never fully substantiated. The rarity of carcinoma as a sequel is a further point of distinction from Menetrier's 'polyadenome polypeux', in which the tendency to malignant change is well known.

Though in our case the lesion had been taken for a carcinoma pre-operatively there were features which lent uncertainty to this diagnosis and gastroscopy was considered. It was not undertaken, however, partly from conviction that laparotomy would be necessary anyway on account of the recurrent hæmorrhage, partly because the lesion was known to border on the cardia and to have caused dysphagia, and partly because the ulcer craters led us mistakenly to omit consideration of Menetrier's disease in the diagnosis. We now believe that in view of the first radiological report with its clear hint of rugal hypertrophy, gastroscopy should have been attempted. It could have been done immediately before beginning the laparotomy, so that operation could have been cancelled or continued with in the light of the findings or had the manœuvre caused the onset of fresh bleeding.

In our case the gastroscopic appearance might not, as it happens, have been helpful, even had a view been obtainable, for the swelling and mamillation surrounding the ulcer craters would have looked through the gastroscope very suggestive of malignancy.

The finding at laparotomy of a soft tumour in the stomach, especially a sausage-shaped one, should have prompted us to open the stomach for inspection before deciding upon resection, for the discovery of giant rugal hypertrophy might have led us to decide upon a different course of action. Had we known as we do now that a resection across hypertrophied folds leads to a very difficult and precarious anastomosis we should have realized that a total gastrectomy might be the least dangerous kind of resection in such a case; but we might have hesitated to undertake so much, even though repeated hæmorrhage had been one of the indications for operation, for giant rugal hypertrophy is not necessarily, *per se*, an indication for gastrectomy, much less a total one.

Having committed ourselves to resection, however, before the true nature of this rare lesion was appreciated, we might have done better to remove the rest of the abnormal stomach as well, and then put in a pedicled segment of jejunum to connect œsophagus to duodenum.

Had we made the correct diagnosis in time, but been forced to operate by uncontrollable hæmorrhage, we might have attempted resection of only the affected parts of the stomach, refashioning what was left into some sort of bag as best we were able.

* Exactly what these were is not stated by the authors (Kenney and others, 1954), but apparently two patients had pituitary tumours, in one case combined with multiple parathyroid adenomas and possibly also an islet-cell adenoma.

BIBLIOGRAPHY

FORRESTER-WOOD, W. R. (1950), *Brit. J. Surg.*, **37**, 278.

GOODALE, F. jun., and SNIFFEN, R. C. (1953), *New Engl. J. Med.*, **249**, 1105.

HEWER, T. F. (1954), *Sem. Hôp. Paris*, No. 4, 167.

KENNEY, F. D., DOCKERTY, M. B., and WAUGH, J. M. (1954), *Cancer*, **7**, 671.

MATZNER, M. J., RAAB, A. P., and SPEAR, P. W. (1951), *Gastroenterology*, **18**, 296.

MENETRIER, P. (1888), *Arch. Physiol. norm. path.*, **1**, 32 and 236.

SPRIGGS, E. I., and MARXER, O. A. (1943), *Quart. J. Med.*, **12**, 1.

Weekly Clinicopathological Exercises (Cabot Case No. 40451) (1954), *New Engl. J. Med.*, **251**, 823.

EXPERIMENTAL SURGERY

RESUSCITATION OF THE K-ARRESTED HYPOTHERMIC HEART

AN EXPERIMENTAL STUDY

By G. E. MAVOR, R. K. McEVOY, R. A. HARDER, and E. B. MAHONEY

FROM THE ROCHESTER UNIVERSITY SCHOOL OF MEDICINE AND DENTISTRY

THERE is some evidence that the myocardium loses potassium during induction of general hypothermia to 25° C. (Covino and Hegnauer, 1955; Olsen, Rudolph, and Gollon, 1955). If circulatory arrest is undertaken by caval occlusion this trend is accentuated (Mavor, Harder, McEvoy, McCoord, and Mahoney, 1956). Furthermore, it has been recognized for some time that during ventricular fibrillation potassium leaves the heart in considerable quantities (Kehar and Hooker 1935; Montgomery, Prevedel, and Swan, 1954). The administration of potassium in high concentrations will conveniently depress all myocardial activity and arrest the heart (Howell, 1905; Wiggers, 1930; Thomson, 1939; Winkler, Hoff, and Smith, 1939; Fenn, 1940), and its use in this way in hypothermia might also serve to replenish the depleted myocardium. Accordingly potassium has been used to induce arrest both at the outset of caval occlusion and at the end as an initial step in resuscitation, and results as regards heart and dog recovery have been satisfactory (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). Furthermore, it would seem that the only worthwhile method of correction of ventricular fibrillation would entail the administration of potassium. Swan, Zeavin, Blount, and Virtue (1953) have used potassium successfully as a defibrillator for some years, employing calcium chloride in resuscitation as Wiggers (1930) described. This has also been our experience, although calcium has not been found necessary (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). However, there is no doubt that the use of potassium to induce arrest in the presence of either sinus rhythm or ventricular fibrillation is only worth considering if a satisfactory method of resuscitation is feasible.

The purpose of this paper is to report a method of resuscitation utilizing cardiac massage, 50 per cent glucose, and insulin. Other observations pertaining to successful recovery from potassium arrest are also reported.

METHOD

In 27 fasting (overnight) mongrel dogs of an average body-weight of 17 kg., hypothermia was induced to a rectal temperature of 26° C. in an ice-water bath at 4° C. Pentothal sodium anæsthesia was used in all cases, the initial average dose being 16 mg./kg. This drug was also used to maintain a light anæsthesia before surface cooling and to control shivering during cooling: the latter required 50–100 mg. on each occasion. The average total dosage was 700 mg. After endotracheal intubation respirations were controlled at the rate of 24 per minute, using intermittent positive-pressure oxygen. During cooling, which averaged 35 min. for the 27 dogs, a CO_2 absorber was added to the closed circuit. Blood samples were removed for arterial CO_2 estimations throughout the experiment.

After removal from the water-bath, a right thoracotomy was carried out with mobilization and control of the venæ cavæ, and ligation of the vena azygos. Thereafter the pericardium was opened and control of the ascending aorta established. During the operative procedures which required 50–60 min., the average temperature drift was 3·3° C. After resuscitation rewarming was carried out to 37° C. in a hot water-bath at 47° C.

Table I.—DETAILS OF POTASSIUM ARREST, CAVAL OCCLUSION AND RECOVERY IN 23 DOGS

Glucose Administration (No. of Dogs)	Time of K Arrest			Caval Occlusion			Recovery	
	With Vent Fibrillation	Caval Occlusion At Outset	Caval Occlusion At End	Duration in Minutes 1–10	11–20	21	Heart	Dog
Given at 'correct' time (14)	3	5*		—	3	—	3	2
				1	4	—	5	5
			6	1	5	—	6	6
Given at 'incorrect' time (9)	3			1	2	—	3	3
		4		1	2	1	4	3
			2	1	2	—	2	1
Total (23)							23	20

By 'correct' time is indicated 'responsive phase'.
* All five dogs had right ventriculotomies.

Polyethylene catheters had been previously inserted via the left femoral artery and vein, the former being threaded to lie in the ascending aorta, the latter in the inferior vena cava. Arterial and venous pressures were recorded by means of two Statham strain gauges connected to a continuous poly-Viso four-channel Sanborn recorder. 100 c.c. of heparinized whole blood were given intra-arterially

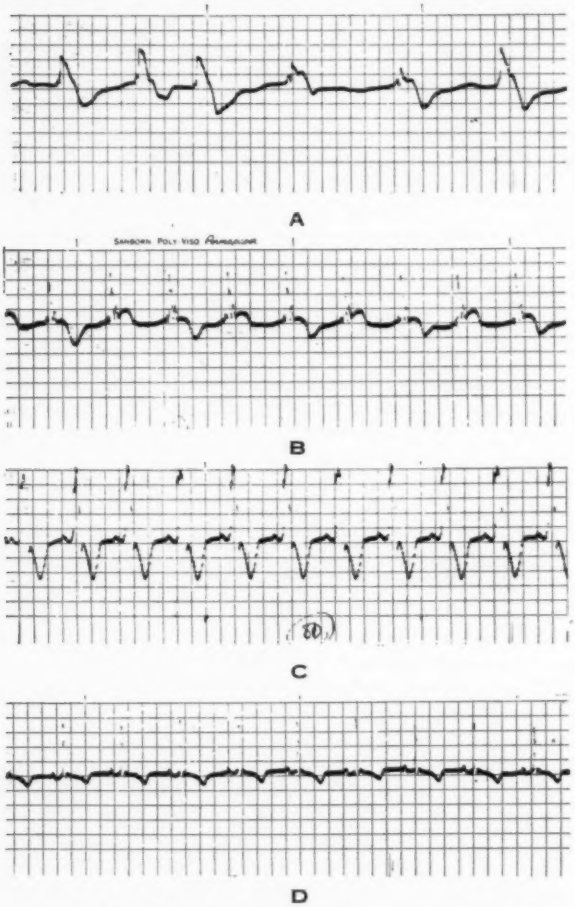


FIG. 649.—E. C. G. showing changes in absence of initial i.v. 50 per cent glucose, despite small dose of potassium, and improvement after glucose administration. Dog 55–228, received 8 mEq. K, 20 ml. i.v. 50 per cent glucose, no insulin. Caval occlusion time 15 min. Ventricular recovery time 4 min. A, Time 1.29 p.m. Early ventricular complexes 4 min. after end of caval occlusion, plasma K 7·9 mEq./l., arterial and venous pressures 40 and 7 mm. Hg, rate 46 per min. B, Time 1.30 p.m., plasma K 6·4 mEq./l., arterial and venous pressures 46 and 6 mm. Hg, rate 75. At 1.30 p.m. 20 ml. i.v. 50 per cent glucose given. C, Time 1.32 p.m., arterial and venous pressures 90 and 3·5 mm. Hg, rate 85. D, Time 1.34 p.m., arterial and venous pressures 86 and 4 mm. Hg, rate 74. Improvement in E. C. G. with return to normal intraventricular conduction time.

at the end of the period of inflow tract occlusion and 10 c.c. of 1 per cent protamine sulphate intravenously during chest closure. Arterial samples were taken for plasma-potassium and -glucose levels. No intravenous fluids were administered.

Intermittent electrocardiographic recordings (25 mm. per sec. and 1 mv. per cm.) were taken throughout each experiment with right fore-leg and right and left hind-leg leads.

Potassium was administered as KCl solution, 1 mEq./ml. at *p*H 5·6. With occlusion of the inflow tracts the solution of KCl was injected into the first part of the ascending aorta, which had been clamped distally. In this way perfusion of the coronary arterial system was obtained, aided by cardiac massage. The KCl solution was slowly injected in quantity sufficient to cause complete electrocardiographic arrest.

Plasma K was determined with the Baird flame photometer, using the internal standard lithium.

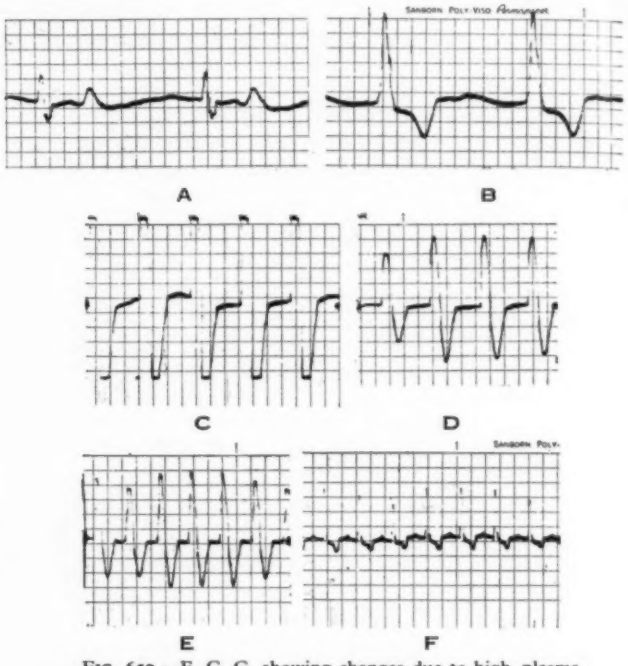


FIG. 650.—E. C. G. showing changes due to high plasma-potassium level and improvement after glucose administration. Dog 55–196, received 68 mEq. K, 50 ml. i.v. 50 per cent glucose, no insulin. Caval occlusion time 15 min. A, Time 2.10 p.m., ventricular complexes 8 min. after onset of idioventricular rhythm and initial 40 ml. 50 per cent glucose. Plasma-K 7·2 mEq./l., arterial and venous pressures 56 and 8 mm. Hg, rate 30 per min. B, Time 2.25 p.m., plasma-K 6·4 mEq./l., arterial and venous pressures 56 and 8 mm. Hg, rate 30. Rewarming then took place in water bath at 47° C. C, After rewarming. Time 3.35 p.m., plasma-K 6·8 mEq./l., arterial and venous pressures 98 and 7 mm. Hg, rate 80. D, Time 3.45 p.m., rate 84. 20 ml. 50 per cent glucose i.v. at 4.48 p.m. E, Time 4.50 p.m., arterial and venous pressures 120 and 5 mm. Hg, rate 136 per min. F, Time 5.00 p.m., plasma-K 4·6 mEq./l., arterial and venous pressures 115 and 3 mm. Hg, rate 130. E. C. G. shows return of P wave and sinus rhythm. Uneventful recovery.

For the estimation of glucose a filtrate was prepared by the micro Folin-Wu technique, and the concentration of glucose was then determined by Benedict's colorimetric method.

Procedures.—Bulldog clamps were used to occlude the venæ cavæ when arrest of the circulation was required. The pulmonary vessels and ascending aorta were not clamped, except in the case of the latter when potassium was being given.

The 27 dogs were all subjected to varying periods of caval occlusion and all underwent potassium-induced cardiac arrest. In 6 dogs arrest followed ventricular fibrillation of varying periods, and in the remainder it was induced in the presence of sinus rhythm (*Table I*). In all cases resuscitation was commenced by cardiac massage immediately after the release of inflow tract occlusion, and each dog received intravenous glucose thereafter: 14 dogs received insulin during recovery, and in 4 either

sucrose or choline chloride was used as an alternative to glucose in intitial resuscitation. During caval occlusion right ventriculotomy was performed in 5 dogs, and right auriculotomy in 8.

THE ADMINISTRATION OF 50 PER CENT GLUCOSE AND INSULIN

The aim of potassium administration prior to commencing resuscitation was to produce electrocardiographic arrest. Clinical observation of cardiac

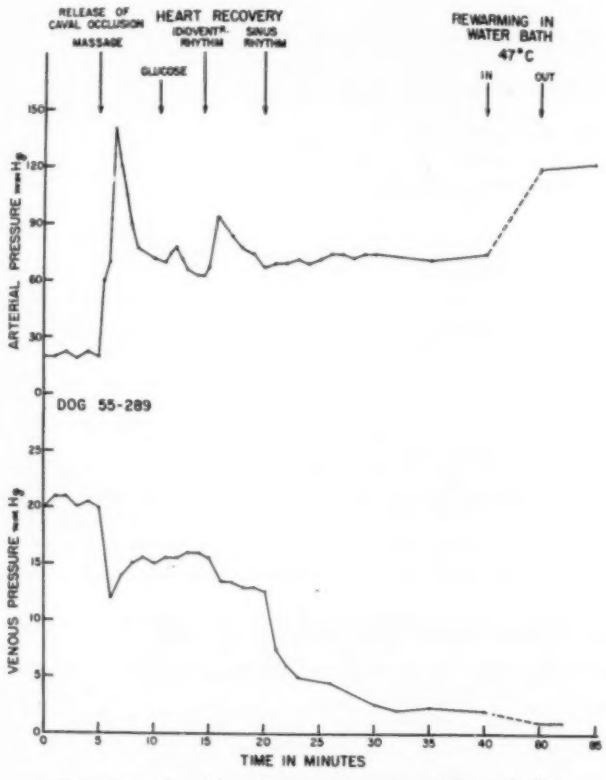


FIG. 651.—Arterial and venous pressure changes during resuscitation from potassium-induced cardiac arrest. The rises in arterial pressure are associated with (*a*) massage and the vasopressor effect of potassium, (*b*) intravenous 50 per cent glucose, and (*c*) the onset of idioventricular rhythm. The significant falls in venous pressure follow the onset of (*a*) idioventricular rhythm and (*b*) sinus rhythm.

arrest was not accurate, and if total depression of all myocardial functions did not occur, portions of the ventricles escaped and served as foci for ectopic activity, so that slow 'wave' fibrillation resulted soon after massage was instituted (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). The sequence of events following the institution of massage after potassium arrest has been recently described (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). In most cases after a period of potassium asystole and prior to the establishment of idioventricular rhythm, a 'responsive phase' arises, when the ventricles contract only after the stimulus of touch or of massage, particularly of the septal area, and after contraction become asystolic. Idioventricular rhythm is then established. In some cases, however, without or after a 'responsive phase' of short duration, 'wave' fibrillation occurs, and can only be abolished by a second and larger dose of potassium. Mainly because of this, resuscitation by massage alone following potassium arrest, though usually finally successful, was unreliable and on occasion took a long time and multiple doses of potassium.

Although by massage alone the concentration of potassium in the extracellular tissues of the heart could be slowly lowered, it seemed that a more rapid method of eliminating the excess potassium was necessary. In this way sinus rhythm or, failing this,

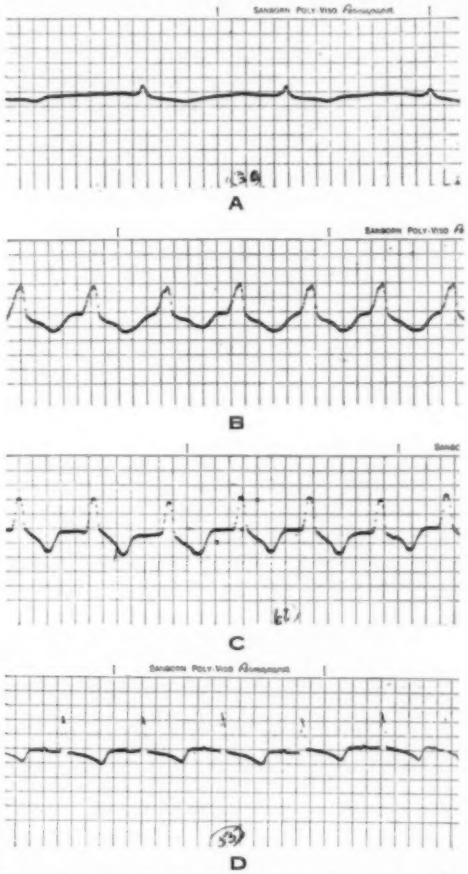


FIG. 652.—E. C. G. showing rapid recovery after satisfactory glucose resuscitation from potassium arrest. Dog 55–218 received 20 mEq. K, 40 ml. i.v. 50 per cent glucose, 20 units insulin. Caval occlusion time 18 min. Ventricular recovery time 7 min. A, Time 1.02 p.m., early ventricular complexes, arterial pressure 95 mm. Hg, rate 30 per min. B, Time 1.03 p.m. idioventricular rhythm, active phase of ventricular recovery, arterial pressure 100 mm. Hg. C, Time 1.04 p.m., idioventricular rhythm, but good atrial contractions clinically. D, Time 1.11 p.m., sinus rhythm with first degree A–V block, arterial pressure 67 mm. Hg. Uneventful recovery.

idioventricular contractions might be quickly restored. Fifty per cent glucose was used in the belief that the osmotic action of a hypertonic solution would have such an effect.

In 23 dogs 50 per cent glucose has been used in resuscitation. It produced great improvement in cardiac action and caused dramatic changes in the electrocardiogram. The former consisted of the establishment of idioventricular rhythm or, when this was already present, the return of atrial contractions, and on occasion successful conversion of potassium induced 'wave' fibrillation to a normal ventricular beat. As regards the electrocardiogram, glucose

abolished or considerably decreased the features in the electrocardiogram usually regarded as due to a high plasma-potassium level (*Figs.* 649, 650).

However, it became apparent in the course of these studies that to be most effective glucose had to be given when the ventricles were ' responsive '. It has been given in 14 dogs at this time and spontaneous ventricular contractions have resulted in all cases within 2–5 min.; 20 ml. of 50 per cent glucose was the dose used. This was given within a period of 15 sec. and was repeated in most cases within 3–7 min. (*Fig.* 651). The atrium during this period of ventricular recovery was usually distended and showed ripple-like contractions which were the result of backspread of the ventricular impulse. As the venous pressure fell (*Fig.* 651) small contractions at the site of the sinus node were seen and these gradually increased in intensity and scope. In cases of delay atrial contractions frequently returned after a further 10 g. of 50 per cent glucose. Eventually good atrial contractions developed and heart-block preceded the onset of sinus rhythm (*Figs.* 652, 653).

Table II.—VENTRICULAR AND E.C.G. RECOVERY TIMES AFTER K ARREST AND GLUCOSE RESUSCITATION IN 14 DOGS

	SINGLE K DOSE WITH ARREST	MULTIPLE K DOSES (Recovery from Last Arrest)	TOTAL AND AVERAGE
No. of dogs	10	4*	14
Ventricular recovery time :—			
Average	8·1 min.	15·2 min.	10·4 min.
Range	4·0 to 12·0 min.	8·0 to 30 min.	4·0 to 30 min.
E.C.G. recovery time :—			
Average	15·8 min.	22·3 min.	17·6 min.
Range	8·0 to 40 min.	17·0 to 30 min.	8·0 to 40 min.

* Each dog received two doses of K, but was subjected to only 1 E.C.G. arrest.

Following the intravenous injection of glucose, the heart improved in tone and in the vigour of its contraction following massage. A rise of arterial pressure was common at this stage (*Fig.* 651). Thereafter idioventricular rhythm resulted (*Fig.* 652). The ventricles passed through a phase of greatly increased activity soon after spontaneous activity returned, their rate and the arterial pressure being much in excess of that expected at the current temperature (*Figs.* 651, 652). After this phase of activity ventricular action and arterial pressure subsided an electrocardiogram approaching the control taken before arrest, 14·9 min. (*Table II*). The rapid recovery of the electrocardiogram was a striking feature of glucose resuscitation. Moreover, apart from the time factor, the pattern of recovery was more

In these 14 dogs the ventricular recovery time, which was the time from the end of caval occlusion until the maintenance of an effective arterial pressure, averaged 10·2 min., and the electrocardiographic recovery time, which was the time from the end of caval occlusion to the presence of sinus rhythm and

Table III.—PLASMA-POTASSIUM AND -GLUCOSE LEVELS DURING COOLING, CAVAL OCCLUSION AND RESUSCITATION FROM POTASSIUM ARREST—WITH USE OF INSULIN (DOG 55–302)

TIME	TEMPERATURE	PLASMA-K	PLASMA-GLUCOSE	HEART
(Min.)	(° C.)	mEq./l.	mg. per cent	
0	36·0	4·2	86	Sinus rhythm; Rate 140 Arterial pressure 140
		Cooled in water bath at 4° C.—30 min.		
35	29·7	4·0	76	Rate 66
		Thoracotomy and mobilization of vessels —75 min.		
116	24·0	4·0	176	Rate 62
125	24·0		188	Rate 62
		Occlusion of cavæ and aorta—3 min. KCl 10 mEq. intra-aortic		
131	24·0	12·7	196	Arrest
133	24·0	9·8	196	Massage
135		Glucose 10 g. i.v.		' Responsive phase '
138	24·0	6·8		Idioventricular rhythm
140		Glucose 10 g. i.v.; insulin 20 units i.v.		
145	24·0	5·28	1140	Sinus rhythm
165	24·4	4·0	924	Rate 56
185	24·4	3·72	680	Rate 58
195	25·0	Chest incision closed		Rate 60
		Rewarming in water-bath at 47° C.—45 min.		
205	27·2	3·72	410	
225	33·3	4·0	264	
240	35·6	Removed from warming bath		
245	35·8	4·0	84	Rate 132 Arterial pressure 120
Dog 55–302				

regular as compared to that following resuscitation from potassium arrest without glucose (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956).

Once resuscitation to spontaneous heart action had been achieved, a high persistent potassium level in the range 6·2–8·4 mEq./l. could compromise recovery by bringing about deterioration in heart action. This could be followed on the electrocardiogram (*Fig.* 650), and was associated with falling arterial and rising venous pressures. Eventually arrest might recur. This occurred in one case in this series. The total

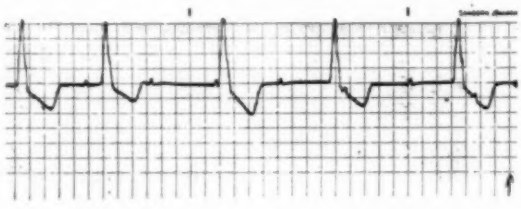


FIG. 653.—E. C. G. showing complete heart block during recovery from potassium arrest. Dog 55–166.

potassium dose was 54 mEq. Cardiac arrest occurred during rewarming, the plasma-potassium level being 6·4 mEq./l. However, this deterioration in the electrocardiogram could be quickly halted by the administration of further glucose (*Figs.* 649, 650). With the usual potassium dose required to produce arrest there is no such danger, and quantities of potassium up to a total of 30–40 mEq. have been readily tolerated. In the presence of high potassium

SUCROSE AND CHOLINE EFFECTS

In an endeavour to confirm that the effects of 50 per cent glucose on restoration of spontaneous ventricular contractions were due to the hypertonicity of the solution, sucrose and choline chloride

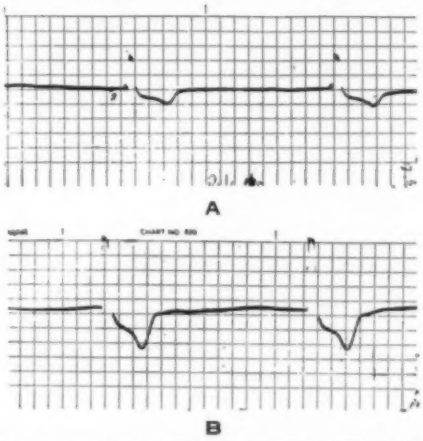


FIG. 654.—E. C. G. showing recovery following the use of choline chloride in place of 50 per cent glucose. Dog 55–257. A, Time 12.35 p.m., idioventricular rhythm, arterial and venous pressures 72 and 15 mm. Hg, rate 20 per min. B, 12.40 p.m., no great change in E. C. G., arterial and venous pressure 56 and 18 mm. Hg.

were used as an alternative to glucose in 4 dogs. The quantities employed, equal osmatically to 10 g. of glucose, consisted of 40 c.c. of 50 per cent sucrose,

Table IV.—PLASMA-POTASSIUM AND -GLUCOSE LEVELS DURING COOLING, CAVAL OCCLUSION AND RESUSCITATION FROM POTASSIUM ARREST—WITHOUT USE OF INSULIN (DOG 55–204)

TIME	TEMPERATURE	PLASMA-K	PLASMA-GLUCOSE	HEART
(Min.)	(° C.)	mEq./l.	mg. per cent	
0	36·1	4·10	86	Sinus rhythm ; Rate 214 Arterial pressure 154
		Cooled in water bath at 4° C.—40 min		
48	28·9	3·00	68	Rate 82
		Thoracotomy and mobilization of vessels		
155	25·5	2·70	78	Rate 82
		Three minute occlusion of cavæ		
173	25·5	4·80	116	Rate 75
		Three minute occlusion of cavæ		
182	25·5	4·50	122	Rate 75
		Three minute occlusion of cavæ		
188	25·5	4·70	158	Rate 76
195		KCl 8 mEq. intra-aortic ; massage		
197		KCl 12 mEq. intra-aortic ; massage		
208	25·8	14·60	212	Massage
210		Glucose 10 g. i.v.		' Responsive phase '
213		7·82		
214		Glucose 10 g. i.v.		Idioventricular rhythm
218	26·1	4·40	980	Sinus rhythm ; Rate 60
238		4·20	890	Rate 60
258		4·12	836	Rate 60
260	26·4	Chest incision closed		
		Rewarming in water bath—45 min		
310	35·0	3·84	642	Rate 160 Arterial pressure 145

dosage, usually of a multiple nature, the plasma level was easily controlled by giving insulin and further glucose (*Table III*). As a rule 20 units of crystalline insulin were given after restoration of cardiac action. This was repeated at the end of an hour along with further glucose if this was indicated. If insulin was not given high glucose levels persisted for some hours (*Table IV*).

and 25 c.c. containing 3·9 g. of choline chloride. These were given when the ventricles were in the ' responsive phase ' and once again shortly afterwards.

The effects of these solutions paralleled those of 50 per cent glucose in establishing spontaneous ventricular contractions, and in all 4 cases cardiac recovery was achieved. In one case atrial contractions

were restored where these had been absent after idioventricular rhythm of some duration. Co-ordination of ventricular activity was obtained in another case where the ventricle although contracting after massage was showing a continuation of the contraction wave. After successful cardiac resuscitation, deterioration occurred in the electrocardiogram (*Fig.* 654) as was expected in the absence of glucose.

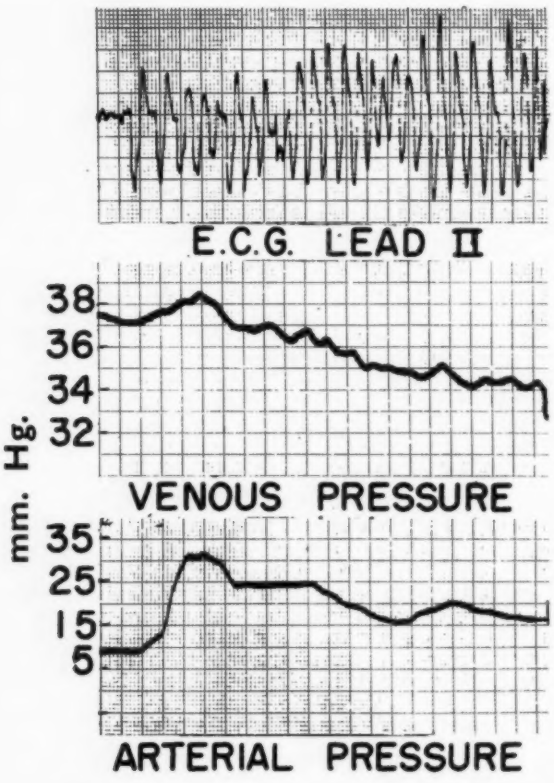


FIG. 655.—Arterial and venous pressure changes after removal of occlusion clamp on superior vena cava and institution of cardiac massage. Fall of venous pressure from 38·5 to 34 mm. Hg, and of arterial pressure (despite cardiac massage) from 30 to 15 mm. Hg. E. C. G. shows massage pattern.

All 4 dogs died. The dogs receiving sucrose died 12 and 28 hours post-operatively. There were no significant post-mortem findings. In the dogs which received choline chloride, an acetylcholine-like effect developed, an extreme bradycardia persisting (*Fig.* 654) despite temporary correction by atropine. Areflexia and total depression of the central nervous system was also present and the dogs died from these toxic effects.

CARDIAC MASSAGE AND VENOUS PRESSURE CHANGES

The clamps on the superior and inferior venæ cavæ were removed quickly and massage instituted. It was interesting that after removal of the superior vena cava clamp there was often a fall in the inferior vena cava pressure (*Fig.* 655). However, with only this clamp removed, massage did not provide an effective arterial pressure (*Fig.* 655).

After release of both inflow tract occlusion clamps, the venous pressure fell quickly, but stabilized at a level much higher than control values (*Fig.* 651). A great fall in venous pressure at this time to levels approaching normal was always a bad prognostic sign and represented the first indication of existing peripheral failure or shock. Only thereafter would the persisting low arterial pressure convey this information. Normally the arterial pressure shortly after the commencement of massage rose to high levels (*Fig.* 651) as a result of the vasopressor action of injected potassium.

The usual high venous pressure during massage retarded atrial recovery. Atrial distension was often noted to cause deterioration in atrial contractions followed by arrest. Furthermore it was interesting that after such an event caval occlusion to allow a drop in atrial pressure might restore atrial contractions. Carried out along with ventricular massage, atrial massage, which prevented gross distension of the atrium although it did not lower the venous pressure, often facilitated the return of atrial activity. This was important as it might hasten the return of sinus rhythm. Ventricular massage, though effective in maintaining an adequate arterial pressure, was incapable of lowering the venous pressure (*Fig.* 651). This was a constant finding. However, whenever spontaneous ventricular action occurred, the venous pressure fell (*Fig.* 651). This fall in venous pressure was sometimes delayed, but always heralded the return of vigorous atrial activity, and then sinus rhythm, and became a good prognostic sign as regards final heart recovery.

It was always important to maintain oxygenation of the myocardium by massage until the contracting ventricles were producing an effective arterial pressure. Too early cessation of massage at this time compromised cardiac recovery. No danger emanated from continuing massage even after the ventricles were maintaining an adequate pressure.

INTRA-ARTERIAL BLOOD

The need to avoid any unnecessary increase in venous pressure during the period of cardiac massage led to the practice of giving all blood intra-arterially. When required, blood was given into the ascending aorta after removal of the caval clamps. It was noted that when blood was given intravenously at the same speed, there was a sharper and greater rise in inferior vena cava pressure than when given intra-arterially, although this variation in response did not persist and final values for venous pressures were the same irrespective of the route of transfusion.

The timing of blood transfusion after removal of the caval clamps was designed to aid oxygenation of the myocardium, although there appeared no indication for blood prior to circulatory arrest. No intravenous fluids were given during cooling or the operative procedure, as their administration was related to a greatly increased incidence of post-operative pulmonary complications, a fact also noted by Cookson (1955).

PERICARDIAL CLOSURE

During cardiac arrest without massage and during ventricular fibrillation, the heart may dilate. It is important to prevent this either by caval occlusion or manual control of the heart as the situation demands. After successful restoration of cardiac action some cardiac enlargement may persist and may cause

difficulty in pericardial closure. This cardiac dilatation is probably eventually corrected, but not at a time early enough to allow unrestricted routine closure of the pericardium. In several dogs after pericardial closure, the electrocardiogram rapidly deteriorated, the arterial pressure falling and the venous pressure rising (*Fig.* 656). In one case this sequence of events proceeded to ventricular arrest although atrial activity persisted. Reopening of the

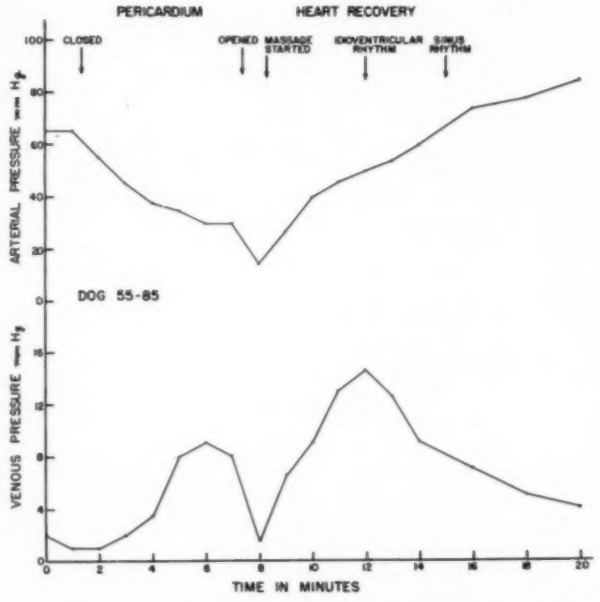


FIG. 656.—Arterial and venous pressure changes after closure of the pericardium and following re-opening and the institution of cardiac massage.

pericardium and cardiac massage restored heart action and in time reversed the pressure trends (*Fig.* 656).

It became the practice to leave the pericardium open in all cases, and no harm resulted from this.

DOG RECOVERY

Of the 23 dogs in this study (4 dogs which received sucrose and choline chloride are excluded), 3 did not survive beyond a 24-hour post-operative period (*Table I*). One suffered a tear of the ascending aorta and died of blood-loss during rewarming. The second had a period of cerebral hypoxia of 34 min., the result of prolonged caval occlusion. This dog failed to regain consciousness and died of pulmonary complications 24 hours post-operatively. In the third dog cardiac arrest recurred during rewarming, as already mentioned. The chest was reopened and the heart restarted by massage alone, only for arrest to develop a third time 50 min. later. This dog received inadequate glucose and no insulin.

DISCUSSION

With manual control of the heart established, large amounts of potassium can be tolerated (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). Electrocardiographic arrest is only readily achieved by potassium in large dosage given either into the left ventricle or preferably into the ascending aorta with the latter clamped above the site of the injection, so that a high concentration reaches the heart. It is safer to err on the side of giving too large a dose than too small. The former will only extend the period of ventricular asystole, while the latter will compromise resuscitation as 'wave' fibrillation will undoubtedly occur on instituting massage.

The 'responsive phase' is regarded as a significant event in ventricular recovery. It is associated with an increase in tone and a maintenance of good myocardial colour, but most important of all with a co-ordinated vigorous contraction which is followed by asystole. It is difficult to understand why a 'responsive phase' should arise unless it represents replenishment of the myocardial cell, for it would seem that with a decrease in potassium concentration 'wave' fibrillation would be an inevitable development. The increase in tone may be significant, for a similar phenomenon occurs in smooth muscle as potassium is replenished (Fenn, 1940). It is suggestive too that the 'responsive phase' may follow in some cases only large doses of potassium, when smaller doses given previously, though causing electrocardiographic arrest, resulted in 'wave' fibrillation. In the absence of glucose administration this 'responsive phase' may last a considerable time (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). Apparently initiation of an impulse at the sino-auricular or atrio-ventricular nodes is not possible. However, the stimulus of touch or massage, particularly of the septal area, is adequate to initiate an impulse which brings about a ventricular contraction wave. At this stage the concentration of potassium in the extracellular tissues of the heart can be reduced by the osmotic effect of a hypertonic solution given intravenously, and restoration of idioventricular rhythm results along with dramatic improvement in the strength and co-ordination of ventricular contractions. There are many advantages in using 50 per cent glucose for this purpose, not least being the reduction of a high plasma-potassium level should this arise, as potassium enters skeletal muscle in association with glucose (Harrop and Benedict, 1924; Flock, Bollman, Mann, and Kendal, 1938; Keys, 1938). Insulin will potentiate this movement (Fenn, 1940) and may be necessary in hypothermia where there is some evidence that the utilization of glucose is impaired at low temperatures (Wynn, 1954; Mavor, Harder, McEvoy, McCoord, and Mahoney, 1956). Without insulin high glucose levels will persist, and compromise the osmotic effects of further glucose should this be administered because of deterioration in the electrocardiogram due to a high plasma-potassium level.

In resuscitation from cardiac arrest, intra-arterial blood has some theoretical advantages over intravenous, although there is little doubt that the recovery of arterial pressure is a function not of the route but of the rate of transfusion (Maloney, Smythe, Gilmore, and Handford, 1954). However, the right atrial pressure rises more sharply and to greater heights when the intravenous route is employed (Maloney and others 1954). In resuscitation from blood-loss without attendant cardiac surgery, this has no particular significance and the trend is of short duration and bears no relation to eventual recovery. However, after a period of circulatory arrest it may be important to avoid any measure calculated to

raise the right atrial pressure unnecessarily, however temporarily.

Adequate oxygenation of the myocardium is always essential. It would seem that despite the evidence of possible venous collateral channels between the inferior and superior venæ cavæ, this cannot be achieved after release of only the superior vena cava clamp. Under these circumstances massage will not produce an adequate arterial pressure and it is unlikely that the ventricular contractions present at this phase will be more effective, so that delay in releasing the inferior vena cava occlusion clamp will only prolong the period of myocardial hypoxia. Oxygenation is also greatly aided by the vasopressor effect of injected potassium (Bacq and Rosenbleuth, 1934; Katz and Katz, 1937; Fenn, 1940), and by the timing of blood administration. Hypoxia even of short duration can have gravely deleterious effects. It is most likely to result from too early cessation of massage after the return of idioventricular rhythm, or soon after pericardial closure. After pericardial closure, if this is undertaken, the electrocardiogram should be carefully followed for any evidence of hypoxia. This is often manifested by diminishing amplitude of the QRS complexes, or their inversion or the appearance of extrasystoles. Presumably a tamponade effect develops, preventing adequate diastolic filling with resultant fall in cardiac output.

There is little doubt that the treatment of ventricular fibrillation in hypothermia presents more problems than at normal temperatures. Electrical defibrillation is not as easily achieved (Kirby, Jensen, and Johnson, 1954), although it has been our experience that resuscitation from arrest presents the greater difficulty. Either fibrillation recurred quickly, or, less commonly, the asystole proved difficult to overcome. This is a common experience, and it was under these circumstances that an artificial pacemaker was found useful (Hopps and Bigelow, 1954). Since using potassium to produce arrest, ventricular fibrillation has not proved a problem and successful resuscitation has resulted in ten consecutive cases in which it was induced or occurred spontaneously (Mavor, Harder, McEvoy, Emerson, and Mahoney, 1956). Nevertheless, reports continue in the literature of unsuccessful results with potassium used in this way (Milstein and Brock, 1954; Ross, 1954).

The induction of cardiac arrest in the presence of sinus rhythm at the outset of caval occlusion has obvious advantages as regards attendant cardiac surgery. Of more importance is the protection which arrest affords to the heart in minimizing the effects of hypoxia and carbon dioxide accumulation. These in their turn are probably responsible for the potassium loss that occurs during caval occlusion (Mavor, Harder, McEvoy, McCoord, and Mahoney, 1956). There is some evidence too that cardiac resuscitation is more easily attained if the heart is stopped during circulatory arrest (Lam, Geoghegan, and Lepore, 1955). Clinically, the heart which beats slowly during caval occlusion appears to have the best prognosis as regards recovery, and, recognizing this, prostigmine has been used both experimentally (Montgomery and others, 1954) and clinically (Swan, 1955) with good results to slow the heart during this period. However, there may be theoretical objections to the use of prostigmine, for there is evidence that in both the heart and skeletal muscle the liberation of potassium is facilitated by acetylcholine accumulation (Lehnartz, 1936; Fenn, 1940).

It is of interest that potassium has been used successfully to produce standstill in the treatment of ventricular fibrillation at normal temperatures, resuscitation thereafter entailing the use of calcium (Black and Harken, 1954). Reports, too, have appeared from time to time of the successful use of 50 per cent glucose in resuscitation from cardiac arrest (Gross, 1955). It is possible that 50 per cent glucose performs several functions. The fibrillating heart may become depleted in sugar (Hooker and Kehar, 1933) and this in turn may explain the potassium loss it suffers (Kehar and Hooker, 1935). After arrest has been produced, intracellular replenishment of both glucose and potassium may result from large doses of glucose. Furthermore hypertonic solutions may have a close relationship to muscle contractility. It would seem that at normal temperatures the use of 50 per cent glucose in large doses might have a role in the treatment of cardiac arrest, even when potassium is not used as a defibrillator.

SUMMARY

1. Under general hypothermia, 27 dogs were subjected to varying periods of caval occlusion and all underwent potassium-induced cardiac arrest. In 6 cases this was in the presence of ventricular fibrillation.

2. Resuscitation was undertaken by means of cardiac massage and 50 per cent glucose and insulin intravenously.

3. Recovery to sinus rhythm and a normal electrocardiogram was achieved in all cases.

4. Three dogs died, one as a result of potassium overdose.

5. In 4 dogs sucrose or choline chloride was used as an alternative to glucose in the initial resuscitation.

REFERENCES

BACQ, Z. M., and ROSENBLEUTH, A. (1934), *Amer. J. Physiol.*, **108**, 46.

BLACK, H., and HARKEN, D. E. (1954), *N. Engl. J. med.*, **251**, 45, 85.

COOKSON, B. A. (1955), personal communication.

COVINO, B. G., and HEGNAUER, A. H. (1955), *Circul. Res.* In the press.

FENN, W. O. (1940), *Physiol. Rev.*, **20**, 377.

FLOCK, E., BOLLMAN, J. L., MANN, F. C., and KENDAL, E. C. (1938), *J. biol. Chem.*, **125**, 57.

GROSS, R. E., quoted by ADAMS, R. (1955), *J. Amer. med. Ass.*, **158**, 1026.

HARROP, G. A., and BENEDICT, E. M. (1924), *J. biol. Chem.*, **59**, 683.

HOOKER, D. R., and KEHAR, N. D. (1933), *Amer. J. Physiol.*, **105**, 246.

HOPPS, J. A., and BIGELOW, W. G. (1954), *Surgery*, **36**, 833.

HOWELL, W. H. (1905), *Amer. J. Physiol.*, **15**, 280.

KATZ, G., and KATZ, G. (1937), *J. Pharmacol.*, **59**, 284.

KEHAR, N. D., and HOOKER, D. R. (1935), *Amer. J. Physiol.*, **112**, 301.

KEYS, A. (1938), *Ibid.*, **123**, 608.

KIRBY, C. K., JENSEN, J. M., and JOHNSON, J. (1954), *Surgical Forum*, Amer. Coll. Surgn., **5**, 110.

LAM, C. R., GEOGHEGAN, T., and LEPORE, A. (1955), Clin. Meet. Progr. Amer. Ass. thorac. Surg., 21, 22.
LEHNARTZ, E. (1936), *J. Physiol.*, **86**, 37.
MALONEY, J. V., SMYTHE, C. M., GILMORE, J. P., and HANDFORD, S. W. (1953), *Surg. Gynec. Obstet.*, **93**, 51.
MAVOR, G. E., HARDER, R. A., MCEVOY, R. K., MCCOORD, A. B., and MAHONEY, E. B. (1956), *Amer. J. Physiol.*, **185**, 515.
— — — — — — EMERSON, G. L., and MAHONEY, E. B. (1956), Proc. Surg. Forum Clin. Congr. Amer. Coll. Surgn. Philadelphia: W. B. Saunders Co.
MILSTEIN, B. B., and BROCK, Sir R. (1954), *Guy's Hosp. Rep.*, **103**, 213.
MONTGOMERY, A. V., PREVEDEL, A. E., and SWAN, H. (1954), *Circulation*, **10**, 721.
OLSEN, N. S., RUDOLPH, G. G., and GOLLON, F. (1955), *Fed. Proc.*, **14**, 108.
ROSS, D. N. (1954), *Guy's Hosp. Rep.*, **103**, 116.
SWAN, H. (1955), personal communication.
— — ZEAVIN, I., BLOUNT, S. G., and VIRTUE, R. W. (1953), *J. Amer. med. Ass.*, **153**, 12, 1081.
THOMSON, W. A. R. (1939), *Lancet*, **1**, 808.
WIGGERS, C. J. (1930), *Amer. J. Physiol.*, **93**, 197.
WINKLER, A. W., HOFF, H. E., and SMITH, P. K. (1939), *Amer. J. Physiol.*, **127**, 430.
WYNN, V. (1954), *Lancet*, **2**, 575.

THE SUITABILITY OF SKIN AS A STRENGTHENING MATERIAL FOR VEIN GRAFTS*

AN EXPERIMENTAL STUDY

BY P. H. DICKINSON

DEPARTMENT OF SURGERY, KING'S COLLEGE, UNIVERSITY OF DURHAM

THE replacement of injured and diseased arteries in the human patient by various types of vessel graft has become almost a routine procedure within recent years. Many of the problems relating to the use of these grafts have been investigated, but their eventual fate is still unknown and only a long-term follow-up will supply the answer. However, there is some experimental evidence to support the suspicion that one type of graft, the arterial homograft, may eventually degenerate and calcify or become dilated (Coleman, Deterling, and Parshley, 1955). These preserved homogenous arteries have now been used extensively and, certainly from a short-term point of view, have proved satisfactory. However, quite apart from the question of their long-term suitability, there is the problem of their availability, preservation, and storage. To overcome these drawbacks several investigators have been using plastic prosthetic grafts both experimentally and clinically (Shumacker, Harris, and Siderys, 1955; Deterling and Bhonslay, 1955; Rob, 1955), for they are obviously easy to obtain, store, and sterilize, but their suitability and efficacy have yet to be proved.

Probably the ideal replacement for an artery is a fresh autogenous artery, but this is rarely, if ever, possible and it would seem in the meantime that vein grafts, which are available from the patient himself, merit further consideration and investigation. As the main objection to their use is a tendency to dilate, it would appear a useful line of investigation to determine by what means this dilatation can be prevented.

Several methods of supporting vein grafts have already been described, the grafts having been wrapped in such materials as skin (Sako, 1951), fascia lata (Sako, 1951), pericardium (Johnson, Kirby, and Hardy, 1953), and nylon mesh (Vargas and Deterling, 1953). Of these materials skin had already had an extensive clinical trial in the repair of hernias. It has many advocates (Mair, 1946; Cannaday, 1943) and it has a proved place in the surgery of hernia repair. However, over the years enthusiasm for it has waned, principally because of two obvious disadvantages—namely, the difficulty in sterilizing the skin and the occasional development of cysts from persisting epithelial cells (Strahan, 1951). Apart from these drawbacks it has been shown to be a readily available, strong repair material, and because it is a fresh autogenous tissue it has certain advantages over such foreign materials as tantalum gauze mesh and floss silk. Sako (1951) used skin to support autogenous vein grafts in dogs and found infection to be a problem even when the skin used was carefully prepared in situ for five days before operation. In a series of 10 dogs the first 6 died from hæmorrhage due to rupture of the vein graft; in each case there was evidence of infection of the grafts. Penicillin was given systemically to the next 4 dogs, 1 of which died from rupture of the graft and again there was evidence of infection; 3 dogs were well after three months, with functioning grafts. Sako gave no information regarding the fate of the epithelial elements of the skin-grafts.

Skin seemed to possess possibilities as a supporting tissue for vein grafts if the infection and cyst formation could be overcome. It was decided to investigate the suitability of skin for this purpose in a series of experiments using dogs, special attention being paid to the prevention of infection and the prevention of persistence of epithelial elements.

In early experiments the skin used for grafting was prepared by cleansing in situ with an antiseptic solution. When it became apparent that this technique was leading to bad results because of the introduction of infection, search was made for a suitable substance to sterilize the skin; it was learned that the chemical substance called beta-propiolactone had received experimental and clinical trial as an agent for sterilizing plasma (Mangun, Kelly, Sanders,

* This paper is based on a thesis for the degree of Master of Science in the University of Illinois, U.S.A., which was accepted in January, 1955. The experimental work was carried out in that University during tenure by the author of the Memorial Travelling Scholarship in Surgery from the University of Durham.

Piepes, Wallbank, Hartman, 1951) and for sterilizing arterial grafts removed post mortem without aseptic precautions (Trafas, Carlson, Lo Grippo, and Lam, 1954). This sterilizing agent, the simplest of a chemical group known as the beta-lactones, is virucidal and bactericidal and is said not to interfere with the strength or histological structure of the material sterilized by it. It was therefore decided to include in the study an investigation of the efficacy of this material as a sterilizing agent for the skin.

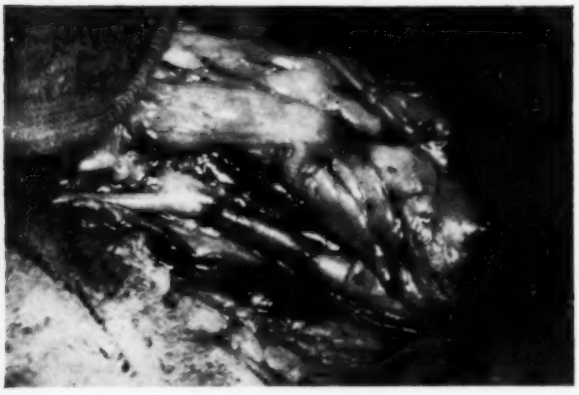


FIG. 657.—Completed vein graft.

FIG. 658.—Dermis wrapped around vein graft.

Various types of skin-graft were used in the preliminary experiments and because dermis seemed the most satisfactory of these it was used exclusively in the later experiments in which beta-propiolactone was used. An interesting and significant feature of this latter study was the influence which beta-propiolactone apparently had on the fate of the epithelial elements of the skin.

MATERIALS AND METHODS

Adult mongrel dogs with an average weight of 31·5 lb. were used. Fifty-eight dogs were operated on and in all of them an autogenous vein graft was placed in a defect made in the abdominal aorta. The average length of the grafts used was 1·9 cm. In 15 dogs whole skin was wrapped around the vein graft; in 12 dogs dermis was used; in 11 dogs epidermis, and in 9 dogs dermis treated with beta-propiolactone. No external support was given to the vein grafts in the remaining 11 animals and these served as controls.

Preparation of Skin-grafts.—Before operation each dog was anæsthetized with morphine (1 gr.) and nembutal (22 mg. per kg. body-weight) injected intraperitoneally, and placed on the operating table in the Trendelenburg position with a sand-bag behind the lower part of the back. The skin of the anterior abdominal wall was shaved and then washed for 5 minutes with soap and water, following which a 1–1000 solution of zephiran chloride was applied.

When a skin-graft was to be used the appropriate type of graft was first taken from the area of the skin incision in the anterior abdominal wall. Whole skin was simply excised, using an elliptical incision. Dermis was excised in a similar manner after the epidermis had been removed with a razor. In both of these types of grafts the subcutaneous fat was removed immediately. The epidermal graft was taken with a razor, the underlying dermis being left in situ and the abdominal incision made to pass through the raw area. The graft was then placed in a sterile solution of saline until the vein graft had been inserted, or prepared with beta-propiolactone in the following way: A solution of beta-propiolactone was made up in isotonic saline as follows: phenol red indicator (5 mg. per 100 ml. of solution), sodium bicarbonate (1·68 g. per 100 ml. of solution), and beta-propiolactone (0·88 ml. per 100 ml. of solution). The dermis was placed in a flask containing this solution and put in a water-bath at 37° C. for 2 hours. At the end of this time the dermis was removed, washed in a sterile phosphate buffer solution (*p*H 7·4) and then in saline, in which it was kept until used. A small piece of the dermis was taken before and after treatment, cut up into small fragments, and put into flasks containing Brewer's thioglycollate culture medium, which were incubated at 37° C. for 72 hours. At the end of this time, or before it, if it was obvious that bacterial growth had occurred in the medium, a subculture was made on a blood-agar plate.

The Operation.—Through a long left paramedian incision the abdominal aorta was exposed and a short segment excised. The whole length of the left common iliac vein was removed and used to replace the aortic deficiency (*Fig.* 657). A simple over-and-over stitch of size 00000 arterial silk was used for each anastomosis. In those experiments where the vein was to be strengthened the skin-graft was cut to the appropriate size and placed around the vein graft and adjacent aorta in one layer with the deep surface innermost. The edges of the skin-graft were united with a continuous 00000 silk suture and at either end the graft was secured to the aortic wall with interrupted silk sutures (*Fig.* 658).

Follow-up Procedures.—Following operation the dogs were placed in individual cages and given normal diet. No antibiotics or anticoagulants were given. The dog's ability to walk was determined and the animal examined for femoral pulses each day for a period of about 7 days after operation and then at intervals until death or sacrifice.

Several of the dogs died either in the early post-operative period or at varying intervals up to 30 days; no dog died after 30 days. The surviving dogs were sacrificed at intervals varying from 37 to 222 days.

When a dog died, a post-mortem examination was carried out as soon as possible. In several cases the graft had ruptured and this was obvious from the presence of a large amount of free blood in the peritoneal cavity and the presence of a clot-filled cavity around the vein graft. The vein graft and adjacent aorta were examined in situ and then removed. The removed specimen was opened, photographed, placed in a 10 per cent solution of formalin, and submitted to histological section. The sections were cut longitudinally and stained (*a*) with hæmotoxylin and eosin, and (*b*) with Weigert's elastic tissue stain.

The surviving dogs immediately prior to sacrifice were again anæsthetized with morphine and nembutal and re-operated on under sterile conditions to allow removal of a portion of the skin-graft and its culture for organisms. In the control animals fibrous tissue from around the vein graft wall was submitted for culture. Great care was taken by changing instruments, gloves, and towels after the graft had been exposed to avoid contamination of the fragments. As with the culture experiments prior to operation, the removed tissue was cut into small fragments and placed in Brewer's medium and incubated, sub-cultured, and then smears made if growth occurred. Meanwhile the exposed aorta was cannulated and 15–20 ml. of a 70 per cent solution of diodrast injected and a radiograph taken. The aortogram was studied to determine whether dilatation or narrowing had occurred in the graft. In several experiments the aortogram was made before opening the abdomen, the diodrast being introduced into the thoracic aorta by needle puncture through the left chest. This procedure was facilitated by a small incision in the left chest through which the left index finger could be inserted to guide the needle point into the aorta. Following aortography the graft was examined in situ, noting in particular any dilatation or narrowing or any visible evidence of the presence of skin. As a final procedure the abdominal aorta and graft were removed and the dog sacrificed. The removed specimen was examined, photographed, and submitted for histological section in the same manner as the specimens removed at autopsy described previously.

All histological preparations were carefully examined microscopically for the presence of epithelium.

RESULTS

The series of 58 dogs operated on is divided into five groups named according to the type of support given to the vein graft. They are, therefore: whole skin, dermis, epidermis, and dermis treated with beta-propiolactone; the unsupported grafts forming a fifth group. The first three groups will sometimes be referred to collectively as the untreated skin group and the fourth as the treated dermis group.

Twelve dogs died within 48 hours of operation, the incidence being approximately the same in each group. The cause of death was not found in these dogs, but in no instance could death be attributed to the type of operation used. One dog in the whole-skin group, 2 in the epidermis group, and 1 in the unsupported group had no femoral pulses from the time of operation, indicating complete block of the graft (*Table I*). Neither these dogs with blocked grafts nor the dogs dying within 48 hours of operation will be considered further. Forty-two dogs survived operation with patent grafts and are available for further study.

Of these 42 dogs, the first 35 operated on either had vein grafts supported with untreated skin or were left unsupported; the remaining 7 were operated on later and had treated dermis as a support. Sixteen died and the others were later killed for study

Table I.—Results Following the Various Methods of Supporting the Vein Graft

Nature of Support for Vein Graft	Functional State of Vein Graft in Dogs which survived the Operation		Number of Dogs which Died within 48 hours of the Operation	Total Number in Each Series
	Patent	Complete Block		
No support	8	1	2	11
Whole skin	10	1	4	15
Dermis	10	0	2	12
Epidermis	7	2	2	11
Treated dermis	7	0	2	9
Total	42	4	12	58

of the grafts. Twelve of the untreated skin group, 1 of the treated dermis group, but none of the unsupported group, died from sudden severe hæmorrhage following rupture of the vein graft. This complication occurred in these dogs between the third and thirty-first post-operative days. The incidence of rupture was approximately the same in

Table II.—Cause of Death in Dogs with Patent Grafts

Nature of Support for Vein Graft	Hæmorrhage following Rupture of Graft	Evisceration	Cause Unknown	Total Number of Patent Grafts
No support	0	0	0	8
Whole skin	5	1	0	10
Dermis	4	0	1	10
Epidermis	3	0	0	7
Treated dermis	1	0	1	7

the three untreated skin groups (*Table II*). As none of the unsupported vein grafts ruptured it appeared that this rupture was related to the presence of the skin, and infection was thought to be the underlying cause. In the animals which died, direct bacteriological proof of infection could not be obtained because even a short delay between death and post-mortem examination may have resulted in falsely positive cultures. At autopsy, though neither peritonitis nor localized suppuration (except in 1 instance) was found, the skin-grafts looked unhealthy and were extremely friable. Subsequent microscopical examination of these ruptured grafts showed the skin to be heavily infiltrated with inflammatory cells (*Fig.* 659). Because of this frequent complication of rupture, probably due to infection, it was decided to try to sterilize the skin before use and then observe whether the incidence of rupture was less.

Bacteriological Findings.—Dermis grafts were used for this part of the experiment. Bacteriological

culture of the dermis prior to treatment with beta-propiolactone was positive in 7 out of 9 grafts (*Table III*). The 2 sterile cultures were presumably due to pre-operative treatment of the skin with soap and water and zephiran which was used routinely in all experiments. All the grafts were found to be sterile immediately following treatment with beta-propiolactone (*Table III*). Further culture experiments on

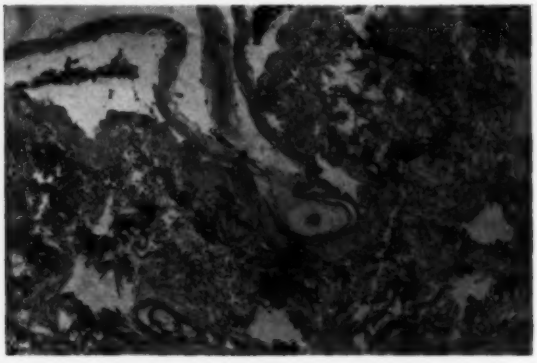


FIG. 659.—Photomicrograph of a whole-skin graft 5 days after implantation. Note the infiltration of inflammatory cells and the apparently degenerating epithelium. H. and E. stain. (× 75.)

samples of 5 of these treated dermis grafts, removed immediately before sacrifice of the animal at periods varying from 37 to 121 days after operation, showed that all of them had remained sterile (*Table IV*). In contrast to this, samples of 11 untreated skin-grafts,

Table III.—RESULTS OF BACTERIOLOGICAL CULTURE OF DERMIS GRAFTS BEFORE AND IMMEDIATELY AFTER TREATMENT WITH BETA-PROPIOLACTONE

Dermis Grafts	*Positive*	*Negative*	*Total*
Before treatment	7	2	9
After treatment	0	9	9

similarly removed but at periods varying from 127 to 222 days after operation, were cultured; all of these 11 specimens were positive (*Table IV*). It could be argued that some of these positive cultures were due to contamination; however, samples of connective tissue from around 7 unsupported vein grafts were subjected to culture in the same manner and all were found to be sterile (*Table IV*).

There were 9 dogs in which vein grafts supported with treated dermis were used; 2 of these died from the operation, whereas the remaining 7 survived with patent grafts. One of the patent grafts ruptured on the eighth post-operative day, giving rise to fatal hæmorrhage. This incidence of rupture of 1 in 7 is to be compared with an incidence of 12 in 27 (or 1 in 2·3) when untreated skin was used (*Table I*).

Macroscopical and Microscopical Findings.—Macroscopical and microscopical examination of the 42 patent grafts was carried out following death or sacrifice of the animal; the youngest being 4 days following transplantation and the oldest 222 days. In addition, a 1-day-old and a 2-day-old treated dermis graft were examined microscopically. In all, the surrounding tissues were adherent to the graft and the adjacent aorta, the degree depending on the time since operation and the type of skin used. In the long-term grafts the degree of adherence was much greater when untreated skin had been used, particularly epidermis. It was felt that the density of the adhesions was an index of the degree of the inflammatory reaction following transplantation.

Untreated Skin Group and Unsupported Group.—Whole skin, epidermis, and untreated dermis could be identified easily with the naked eye in grafts examined within 30 days of operation, but after this time either epithelium was obviously present and

Table IV.—RESULTS OF BACTERIOLOGICAL CULTURE OF UNTREATED, TREATED, AND UNSUPPORTED GRAFTS IMMEDIATELY BEFORE SACRIFICE OF THE ANIMAL

Type of Graft	*Positive*	*Negative*	*Total Examined*
Untreated	11	0	11
Treated	0	5	5
Unsupported	0	7	7

growing, or the whole graft had the appearance of having been converted into fibrous tissue. In all of the whole skin group, and in 3 out of 4 of the epidermis group, visible surface epithelium was

Table V.—INCIDENCE OF SURVIVING EPITHELIAL ELEMENTS IN SKIN-GRAFTS EXAMINED AT PERIODS VARYING FROM 12 TO 222 DAYS FOLLOWING OPERATION

Type of Skin-graft	*Epithelial Elements surviving*	*Total Number examined*
Whole skin	6	6
Dermis	7	8
Epidermis	4	4
Treated dermis	0	6

present in the grafts examined more than 30 days after operation, whereas none was seen in the untreated dermis group. Where surface epithelium was seen it was present only in isolated patches (*Fig.* 660), and there was no adherence between it and the surrounding tissues. In one or two instances there

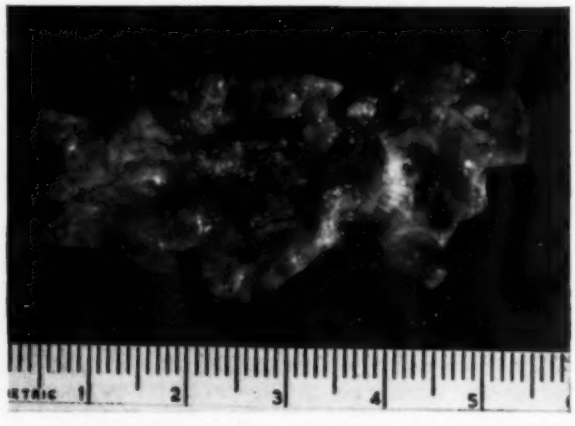


FIG. 660.—External aspect of a vein graft 216 days old supported with epidermis. Note the patch of skin at the centre of the wall.

was an actual space between the skin and the surrounding tissues which contained epithelial debris and hairs. In 2 of the whole-skin group there was a small dermoid cyst containing epithelial debris seen in the vein-graft wall.

Microscopical examination showed that up to the twelfth day following operation the epithelial elements appeared to be undergoing degeneration (*Fig.* 659). Only after the twelfth day could the epithelium be judged to be either living or dead; and

then it was found that living epithelium was present in all but one of the untreated skin group whereas none was present in the treated dermis group (*Table V*).

The number and character of the epithelial elements which persisted varied with the type of skin-graft. In most specimens of the whole-skin group surface epithelium, hair follicles, and sweat glands were present and occasionally sebaceous glands were seen (*Fig.* 661). The 2 cysts seen in this group were lined by typical stratified squamous epithelium (*Fig.* 662). Untreated dermis in most specimens showed hair follicles and sweat ducts (*Fig.* 663). The epidermis grafts showed normal surface epithelium (*Fig.* 664) except in one instance where, in the section examined, there were small cystic spaces lined by epithelium and containing small amounts of debris.

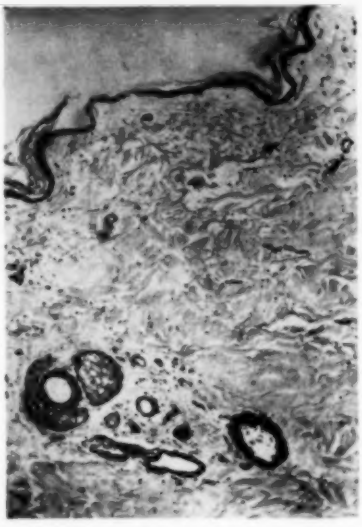


FIG. 661.—Photomicrograph of a whole-skin graft 143 days after implantation. Note the presence of surface epithelium, hair follicles, sebaceous gland, and sweat ducts. H. and E. stain. (× 75.)

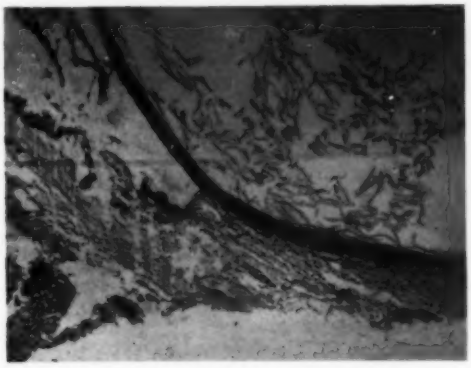


FIG. 662.—Photomicrograph of part of the wall of a dermoid cyst formed in a whole-skin graft 215 days old. Note the normal appearance of the squamous epithelium, and the presence of debris inside the cyst. H. and E. stain. (× 75.)

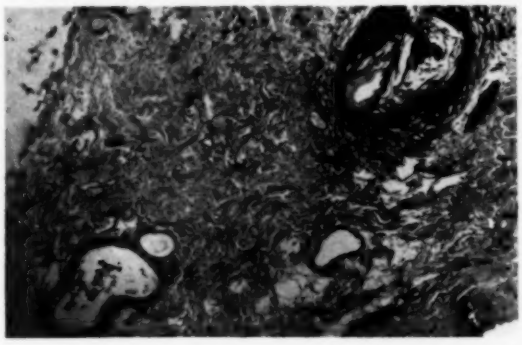


FIG. 663.—Photomicrograph of an untreated dermis graft 161 days after implantation. Note the presence of a hair follicle and of sweat ducts. H. and E. stain. (× 75.)

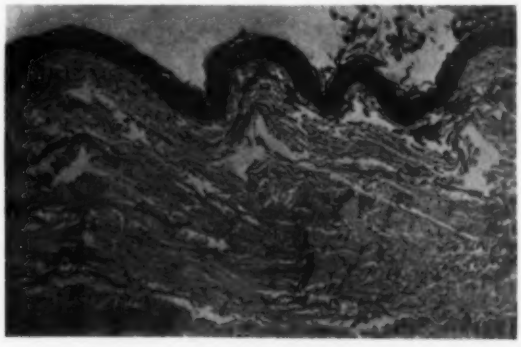


FIG. 664.—Photomicrograph of an epidermis graft 218 days after implantation. The epidermis appears to be growing normally. Note the well-marked fibrous layer between the epithelium and the vein wall. H. and E. stain. (× 75.)

In all of the specimens there was some thickening of the vein wall itself, although it was obvious that a covering contributed appreciably more to the thickness of the wall because only in the unsupported group was the blue colour of the vein still present. Definite dilatation of 2 of the unsupported vein grafts was observed, and some degree of narrowing at the suture lines was present in one or two of each group. Endothelium appeared to be lining all of the grafts but was present only in patches in the earlier ones. It was thickest near the suture lines and often many of the sutures were actually embedded in it (*Fig.* 665). The thickening of the vein wall was seen microscopically to be contributed to by the intima, media, and adventitia (*Fig.* 666).

The thickness and nature of the periadventitia varied with the type of reinforcement used. The unsupported grafts developed quite an appreciable periadventitial layer which, however, contained little or no elastic tissue. In the epidermis grafts a well-marked fibrous layer developed between the epidermis itself and the vein wall (*Fig.* 664), but again this tissue was poor in elastic tissue. Whole-skin and dermis grafts largely took the place of the periadventitia, but in several specimens periadventitial fibrous tissue was seen between the vein grafts and the support. This showed up as a non-staining zone in the sections stained for elastic tissue. In the connective tissue of whole skin and untreated dermis there was always some elastic tissue, but the amount and character were poor. In contrast, however, the elastic tissue of the treated dermis looked quite normal in character and amount in all specimens.

Treated Dermis Group.—The macroscopical and microscopical changes which occurred in the dermis

grafts treated with beta-propiolactone were carefully observed in specimens of the following ages: immediately following treatment, 1 day, 2 days, 8 days, 22 days, 37 days, 92 days, 93 days, 97 days, and 121 days.

Macroscopically, the treated dermis could be identified up to 22 days following operation and it was normal in appearance except in the 8-day-old specimen which had ruptured. In this case the dermis was œdematous and friable. The 37-day-old specimen showed the dermis beginning to lose its identity and becoming fibrous. All the subsequent grafts had tough, thick, fibrous walls in which it was almost impossible to identify the original dermis as such (*Fig.* 667) and at no time was there macroscopic evidence of the persistence of epithelium.

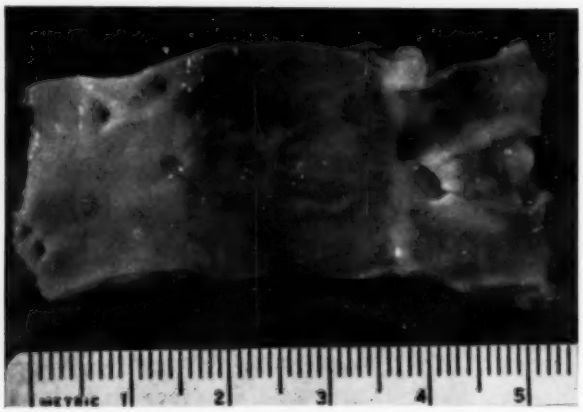


FIG. 665.—Endothelial aspect of a vein graft 92 days old, supported with treated dermis. The majority of the sutures are buried in the newly-formed intima, which is seen to line the entire graft.

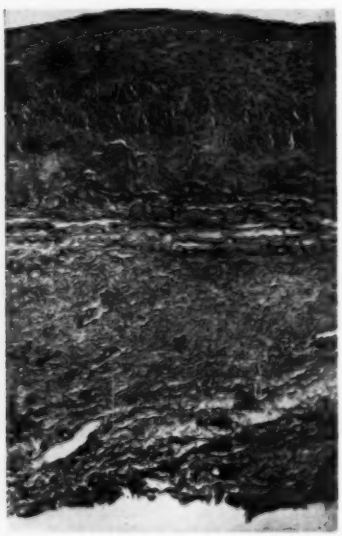


FIG. 666.—Photomicrograph of the wall of an unsupported vein graft 154 days old. The wall is considerably thickened; this thickening involves all layers. H. and E. stain. (× 75.)

For the purposes of clarity the microscopical changes will be described as those affecting the epithelial elements (hair follicles, hairs, and sweat glands) and those affecting the fibrous tissue elements.

The epithelial elements in the specimen of dermis taken immediately after sterilization looked quite normal (*Fig.* 668), but in the 1-, 2-, and 8-day sections the epithelial cell outlines had gone and the nuclei either had disappeared, were fragmented, or showed pyknosis (*Fig.* 669). In the 1-day-old specimen there was a marked invasion of inflammatory cells around the degenerating epithelial structures; there was no such invasion in the 2- and 8-day grafts. In the 22-day specimen the structureless epithelial elements appeared to be breaking up, although the hairs themselves retained their basic architecture. There was a marked collection of lymphocytes, monocytes, and degenerating polymorphs around the remnants of the epithelial elements in the 37-day-old specimen. The 92-, 93-, and 97-day specimens showed numerous hairs, and occasional degenerated hair follicles and sweat glands around which were collected a few histiocytes and some connective tissue.

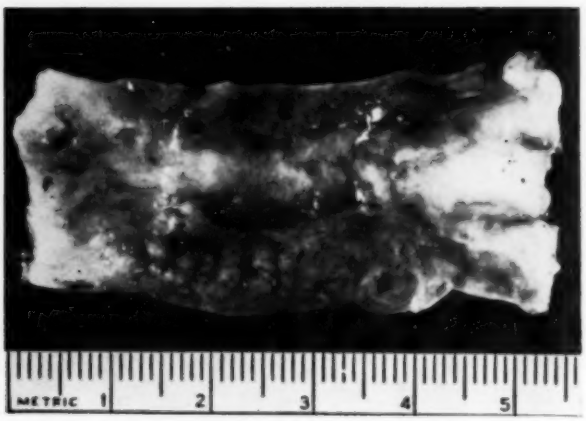


FIG. 667.—External aspect of a vein graft 92 days old, supported with treated dermis. Note that the dermis has almost lost its identity and merges with the surrounding tissues.

In the oldest specimen, 121 days, localized areas of connective tissue were seen, and these were probably at the former sites of epithelial elements now gone.

Table VI.—RESULTS OF AORTOGRAPHY

Type of Vein Graft	*Mild or No Dilatation*	*Definite Dilatation*	*Number of Grafts Examined*
Supported	17	0	17
Unsupported	6	2	8

In other words, it appeared quite definite that the epithelial cells had been killed by the immersion of the dermis in beta-propiolactone; this conclusion appears to be justified since the epithelial cells of dermis grafts not so treated survived without question.

The fibrous elements in the section taken immediately after sterilization were also normal in appearance (*Fig.* 668). However, in the 2-day and 8-day grafts the fibroblasts were reduced in number and those present had extremely deeply stained nuclei; although the actual fibres stained for the most part satisfactorily, those near the surface of the graft showed some evidence of necrosis (*Fig.* 669). In the 22-day-old graft the number of fibroblasts present was further diminished and those present

again showed intense nuclear staining. New connective tissue was seen growing around the graft and at some points penetrating it. The fibrous tissue of the 37-day-old graft showed an almost complete return to normal for there were many healthy-looking fibroblasts between the collagen and elastic fibres. There was again new connective tissue growing into the dermis from outside. This approach to apparent normality was complete in all the later specimens (*Fig.* 670). As mentioned previously, all of these treated specimens had a normal number of elastic fibres and they did not appear to have been affected by the treatment of the graft (*Fig.* 671).

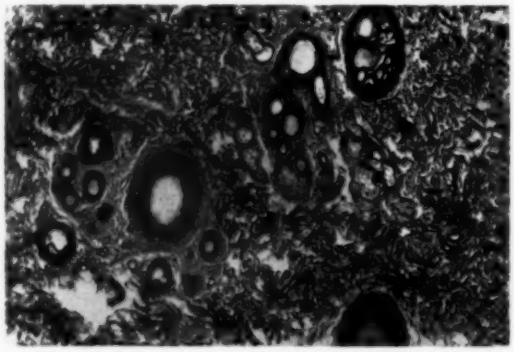


FIG. 668.—Photomicrograph of dermis immediately following treatment with beta-propiolactone. The epithelial and fibrous elements appear normal. H. and E. stain. (× 75.)

Radiological Appearances.—Aortograms were performed in 25 of the dogs with patent grafts at periods varying from 37 days to 222 days after operation. No significant degree of dilatation was found in the supported grafts and dilatation was demonstrated in only 2 of the unsupported grafts (*Table VI, Figs.* 672, 673). However, the follow-up time was short and the series small, so that no conclusions regarding the efficacy of the support can be drawn from these results.

FIG. 670.—Photomicrograph of a vein graft 121 days old supported with treated dermis. The dermis appears normal apart from the absence of epithelial elements. The connective tissue contains a normal number of cells and the fibres stain well. H. and E. stain. (× 75.)

DISCUSSION

The fact that unsupported vein grafts in dogs are apt to dilate can only be suggested by the results of the experiments described because of the short follow-up period involved; however, that such dilatation does occur has been adequately demonstrated by previous workers. The main theme of this discussion is therefore concerned with the suitability of different types of skin-graft for use as supports for vein grafts.

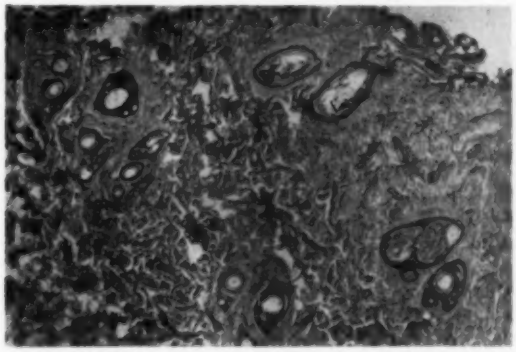


FIG. 669.—Photomicrograph of a treated dermis graft 8 days after implantation. Many of the epithelial cells have lost their nuclei and appear to be degenerating. The number of fibroblasts is diminished, and there is evidence of necrosis of the connective-tissue fibres near the surface. H. and E. stain. (× 75.)

The results of initial experiments of this series showed that vein grafts supported by different types of skin-graft which had only been washed on the surface with soap and water and an antiseptic solution were extremely liable to rupture. At the post-mortem examination of these dogs the skin-grafts were found to be œdematous and friable, and later microscopical study showed that they were heavily infiltrated with inflammatory cells. Although suppuration was found on only one occasion these grafts were considered to be infected. Unfortunately,

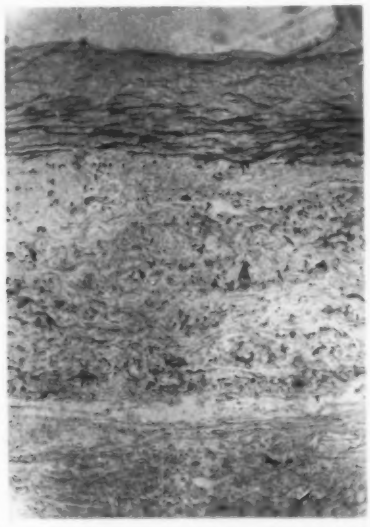


FIG. 671.—Photomicrograph of a vein graft 121 days old supported with treated dermis, stained with Weigert's stain for elastic tissue. The dermis contains numerous elastic fibres whereas the connective tissue outside this contains none. (× 75.)

bacterial cultures of the grafts would not have been of value because of the interval between death and examination. That the presence of the skin plus infection contributed to this high rate of rupture was suggested by the fact that no unsupported vein graft ruptured, and that only 1 of 7 vein grafts supported with treated dermis did so. This improvement in the rupture rate when dermis treated with beta-propiolactone was used as a support is so clear-cut

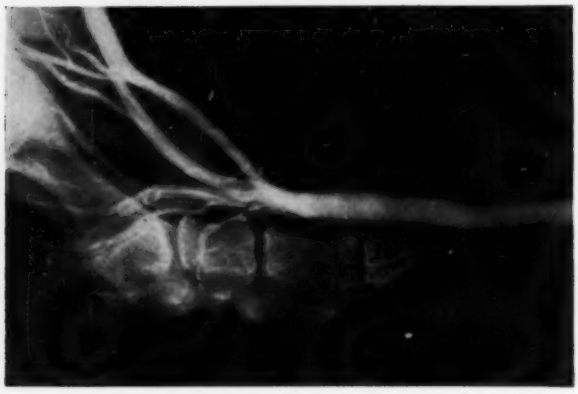


FIG. 672.—Aortogram. Vein graft to abdominal aorta; no dilatation after 92 days. The graft was supported by treated dermis.

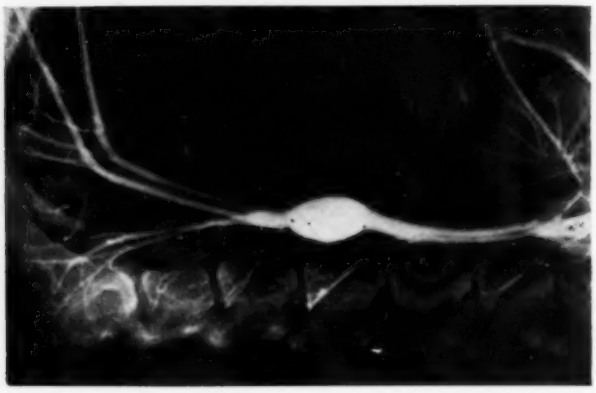


FIG. 673.—Aortogram. Unsupported vein graft to abdominal aorta; definite dilatation after 216 days.

that statistical analysis to estimate its significance was not considered necessary. The cause of the one instance of rupture of a vein graft wrapped with treated dermis was presumably infection, the source of which is uncertain. The dermis was shown by bacteriological culture to be sterile before use and the infection may have been introduced subsequently either by an error in aseptic routine or as a blood-borne infection in the animal. Similar instances of rupture have been reported when other types of graft, such as unsupported vein grafts and arterial homografts, have been used. The presence of organisms in the skin-grafts does not necessarily result in rupture, for in untreated skin-grafts which had been around vein grafts functioning for upwards of seven months living organisms were shown to be present. However, there can be no doubt that their presence constitutes an ever-present threat to the integrity of the vein graft. It is probably not permissible to draw any definite conclusions from this aspect of the experiment and apply them to human surgery because human skin is not so heavily contaminated with bacteria as is dog's skin, and in an operation of this kind a human patient would receive more careful preparation of the skin and be given antibiotic therapy. It would appear, however, to be desirable to use sterile material as a support.

The other hazard of burying skin, so well described by Strahan (1951) and amply confirmed by other workers (Gray, Mansberger, and Yeager, 1951)—namely, the development of cysts and sinuses—was shown to be a potential one in this series of experiments. Although no complications resulted from the presence of living epithelium, they would presumably have occurred in time if the cysts had grown to a large size or if they had become infected. There is a possibility also that this abnormally situated, living skin could give rise to a squamous-cell carcinoma. The continuing growth of the epithelium, as with the persistence of organisms, would appear to be most undesirable.

Hence, it was concluded from this first part of the experiment that untreated whole skin, dermis, and epidermis were unsuitable materials for supporting vein grafts, regardless of their value in preventing dilatation. If skin was to be used as a reinforcing material it appeared that the bacteria and epithelium would have to be destroyed without, if possible, destroying the connective-tissue elements, and it was with this in mind that beta-propiolactone was put to experimental test.

Dermis was selected as the type of skin-graft to be treated with beta-propiolactone because it appeared to be the most favourable of the three types of skin-graft used, in that it probably had the smallest number of organisms and the smallest amount of epithelium, whilst still retaining the fibrous-tissue elements. Immediately following treatment with beta-propiolactone the dermis was found to be sterile, but its appearance did not seem altered in any way either macroscopically or microscopically. That this sterility was not due to any persistence of the chemical in the graft after transfer to the culture medium was shown by the fact that the grafts remained sterile for four months following implantation.

Two factors of importance emerged following the use of treated dermis as a support: one was that the rate of rupture of the vein grafts dropped significantly, and the other was that the epithelial elements in the dermis rapidly disappeared following implantation. Treatment with beta-propiolactone apparently contributed to the destruction of the epithelial cells, but is not held entirely responsible for it; epithelium did persist in all untreated skin-grafts, although the amount remaining in some specimens was small. In other words, as there is a tendency for buried epithelium to degenerate anyway following implantation (the advocates of skin as repair tissue have made a great point of this) it is inferred that the treatment with beta-propiolactone appears to make this tendency a certainty.

Was the structure of the dermis so altered by this treatment, which destroyed its epithelial elements, as to render it an unsuitable reinforcement material? It did not appear to be so, either from a functional or histological standpoint. Although the follow-up

time was short the vein grafts reinforced with this material had tough fibrous walls and none showed any significant dilatation up to four months. Microscopical examination, however, did show some changes apart from the effects on the epithelium. These other changes, which occurred in the fibrous-tissue elements, were difficult to interpret, but it did appear that initially the fibroblasts were affected, for their numbers were diminished and the remaining cells showed nuclear changes. However, after a month or two, by some means or other, the connective tissue of the dermis seemed to recover its normal cellular appearance. Whether these new fibroblasts had arisen from surviving fibroblasts, or whether they had been brought in with new connective tissue which was seen to be growing into the graft, was not determined, and obviously needs further study. At no time did the collagen or elastic fibres show any marked changes from apparent normality.

It can be concluded that dermis following treatment with beta-propiolactone is sterile, contains no living epithelium, and is a thick fibrous material containing elastic tissue. Although its suitability has been demonstrated, its value as a support for vein grafts to prevent dilatation requires further study.

If treated dermis should prove to be a good reinforcement for vein grafts, effectively preventing them from dilating, it is suggested that the method here described would be suitable for clinical application. The extra time and trouble involved in taking the skin-graft and sterilizing it is negligible when compared with the organization and work involved in obtaining, sterilizing, storing, and preparing arterial homografts. This is a particularly cogent point when it is remembered that sufficient long-term studies have not yet been carried out on transplanted homogenous arteries to determine their ultimate suitability, and also when it is remembered that by adopting this method only the patient's own tissues would be used.

SUMMARY

A series of experiments in dogs is described in which the suitability and efficacy of various types of autogenous skin-graft as reinforcing material for autogenous vein grafts to replace part of the abdominal aorta were determined.

Whole skin, epidermis, and dermis grafts, prepared only by routine pre-operative cleansing of the skin, were found to be unsuitable because 12 out of 27 vein grafts supported with one or other of these skin-grafts ruptured. Evidence is presented to support the contention that rupture was due to infection from organisms present in the skin.

The ability of the chemical substance beta-propiolactone to sterilize dermis was studied. All dermis grafts subjected to treatment with this solution were rendered sterile.

This treated dermis being thick, tough, and fibrous was found to be a suitable material for reinforcing vein grafts. Only 1 of 7 vein grafts strengthened with treated dermis ruptured.

Histological studies showed that epithelial elements persisted and grew in untreated skin-grafts, whereas none persisted in treated dermis grafts.

Aortographic studies on all the various grafts showed significant dilatation in 2 of 8 unsupported vein grafts, whereas no significant dilatation occurred in supported grafts.

REFERENCES

CANNADAY, J. E. (1943), *Amer. J. Surg.*, **59**, 409.
COLEMAN, C. C., DETERLING, R. A., and PARSHLEY, M. S. (1955), *Surgery*, **37**, 64.
DETERLING, R. A., and BHONSLAY, S. B. (1955), *Ibid.*, **38**, 71.
GRAY, D. B., MANSBERGER, A. R., and YEAGER, G. H. (1951), *Ann. Surg.*, **134**, 205.
HARTMAN, F. W., PIEPES, S. L., and WALLBANK, A. M. (1951), *Fed. Proc.*, **10**, 358.
JOHNSON, J., KIRBY, C. K., and HARDY, J. D. (1953), *Surgery*, **33**, 207.
MAIR, G. B. (1946), *Brit. J. Surg.*, **34**, 42.
MANGUN, G. H., KELLY, A. R., SANDERS, B. E., PIEPES, S. L., WALLBANK, A. M., and HARTMAN, F. W. (1951), *Fed. Proc.*, **10**, 220.
ROB, C. G. (1955), *Ann. R. Coll. Surg. Engl.*, **17**, 307.
SAKO, Y. (1951), *Surgery*, **30**, 148.
SHUMACKER, H. B., HARRIS, E. J., and SIDERYS, H. (1955), **37**, 80.
STRAHAN, A. W. B. (1951), *Brit. J. Surg.*, **38**, 276.
TRAFAS, P. C., CARLSON, R. E., LO GRIPPO, G. A., and LAM, C. R. (1954), *Arch. Surg., Chicago*, **69**, 415.
VARGAS, L. R., and DETERLING, R. A. (1953), *Surgery*, **34**, 1061.

SHORT NOTES OF RARE OR OBSCURE CASES

SPONTANEOUS HÆMATOMYELIA COMPLICATING PSEUDOHÆMOPHILIA

By F. L. DAVIES

DEPARTMENT OF NEUROSURGERY, THE MIDDLESEX HOSPITAL, LONDON, W.1

SPONTANEOUS non-traumatic hæmatomyelia is a comparatively rare condition (Wyburn-Mason, 1943), but it may occur in a variety of diseases. Kinnier Wilson (1940) reports such aetiological factors as blood diseases and diatheses which include purpura, scurvy, pernicious anæmia, leukæmia, hæmophilia, and essential thrombopenia, arteriosclerotic and syphilitic affections, and aneurysms. Gowers (1903) has described bleeding into a pre-existing syringomyelic cavity; other authors, Dana (1894), and Berkley (1889) have recorded similar cases.

In the series of cases of hæmatomyelia quoted by Wilson (1940) 74 out of 227 cases were classified as spontaneous. In this group, vascular disease accounted for 15 cases, 'congestion' 20 cases, hæmorrhagic diseases 9 cases, and no cause was found in 30 cases. No mention is made of pseudohæmophilia as a cause of hæmatomyelia.

The present case is considered of sufficient interest to merit a full description.

CASE REPORT

HISTORY.—Female, aged 44 years. Married. No children. In childhood she was 'delicate' and was told she was suffering from a 'valvular disease of the heart'. There was no family history of bleeding disease.

1941: She was in the Coventry air raid and was 'shaken up' by several near misses. She developed low back pain, which was diagnosed as spondylitis and was treated by immobilization in a plastic jacket for 2 months.

1947 (*March*): Hysterectomy for menorrhagia performed (at another hospital).

1947 (*August*): Admitted to another hospital suffering from pains in the back, fever, sweating, and petechial spots scattered over the arms and trunk. Examination revealed a raised temperature 100°–101° F., a pulmonary systolic murmur, an enlarged pulmonary artery. E.S.R. 4 mm./hr. W.B.C. 13,000, normal differential, blood-culture negative. A diagnosis of subacute bacterial endocarditis was made, but not confirmed, and treatment consisted of systemic penicillin and oral sulphadiazine. Following her discharge from hospital there were periodic attacks of weakness, malaise, excessive sweating, and left chest pain.

1949 (*October*): Admitted to Middlesex Hospital with a diagnosis of suspected congenital heart disease and bacterial endocarditis. Symptoms consisted of pain in left chest, sweating, malaise, and pyrexia. Petechiæ were scattered over arms and trunk. Pulse-rate 110 per min., T. 99·6, B.P. 135/85. Heart normal in size, systolic thrill over pulmonary area, systolic and diastolic murmurs in mitral area. The spleen was just palpable and the C.N.S. was normal.

Investigations: E.C.G. normal, radiograph of chest normal. Hb 90 per cent (13 g.). E.S.R. 2 mm./hr. (Wintrobe). W.B.C. 5400 normal differential. Platelets 360,000 per c.mm. The temperature reached 99·6° F., with sweating on several days. Blood-culture was sterile on nine successive days. The symptoms gradually subsided and the patient was discharged on Nov. 25, 1949.

1950 (*January*): The patient was in bed at home for five weeks with fever, sweats, and pain in chest and limbs.

1950 (*March*): Onset of pain down the outer side of the left leg, which felt numb and weak; she dragged the foot and had difficulty in getting about.

1950, *Sept.* 18: Readmitted to Middlesex Hospital as an emergency. She complained of a feeling of numbness from the neck downwards, giddiness, and weakness of the arms and legs.

ON EXAMINATION.—Pale slim woman. T. 98·4; Pulse-rate 90 per min., regular; B.P. 115/75. Cardiovascular system as before. Respiratory system: dyspnœa on slight movement, otherwise nothing abnormal found. Nervous system: fully conscious, complete retention of urine. Cranial nerves normal. There was loss of sensation to light touch, pain temperature, and vibration sense up to C.4 level. A profound spastic weakness of all four limbs, including the intercostal and abdominal muscles, was present, all reflexes were exaggerated, left more than right. Plantars both extensor.

Investigations.—Bleeding time 3 min. Clotting time 3½ min. Hb 83 per cent. W.B.C. 7000 normal differential. E.S.R. 60 mm./hr. Puncture pressure 85, complete manumetric block. Protein 60 mg. per cent 1 cell. Lumbar myelogram showed complete obstruction at the C.5, 6 level.

AT OPERATION (Miss D. Beck).—Laminectomy on Sept. 25 (C.4–6). Aspiration of hæmatomyelia of cord. There was a spindle-shaped swelling of the cord which was tightly pressed against the bony laminæ of the 4th, 5th, and 6th cervical vertebræ. The cord did not pulsate below the upper border of the swelling. A needle was inserted into the swelling just to the left of the midline and 3 c.c. of blood was aspirated with prompt disappearance of the swelling and resumption of the pulsation of the cord. The dura mater was left open, a strip of cellophane was laid over the cord, and the closure completed.

At the conclusion of the operation the bleeding and clotting times were normal and the platelet count was 300,000 per c.mm.

POST-OPERATIVE PROGRESS.—Dramatic improvement followed operation. Within six days she was feeding herself and moving all limbs freely. Within fourteen days she was walking. Patient was discharged on Nov. 2, 1950. There were no abnormal neurological signs and she felt better than she had for four years.

The patient attended out-patients yearly, remaining well apart from pains down the left side of the neck, both shoulders, and down the inner sides of both arms.

1956, *April* 12: Patient admitted suffering from severe pain in the left arm, the neck, abdomen, and down the left leg.

ON EXAMINATION.—Patient nervous, sweating, unable to turn in bed without pain in neck and hands. Neck movements painful and limited, especially flexion and extension. Tender over lower cervical spine and left scapula. A few petechiæ over chest. No pallor or cyanosis. Temperature 98·4° F. Cardiovascular system: B.P. 155/100; Pulse-rate 90 per min. Other signs as

recorded on previous admissions. Respiratory system normal. Abdomen: liver just palpable; spleen not palpable. Central nervous system: cranial nerves normal except for bilateral weakness of sternomastoid and trapezii muscles. Limbs: upper limbs hypotonic; power generally diminished in all four limbs; the right triceps muscle weaker than left; movements of legs produced painful spasm of abdominal muscles with nausea. Sensory function: upper limbs normal, patchy analgesia to pin-prick below nipple bilaterally, no loss of thermal sensibility or joint sense. All reflexes brisk and equal, abdominal reflexes absent. Plantars flexor.

Investigations.—Lumbar puncture. Pressure 90 mm. C.S.F. slow rise to 120 mm. C.S.F. and very slow fall; there was a free rise when the neck was extended. Protein 35 mg./100. Globulin slight excess, 1 lymphocyte. Blood examination—Hb 95 per cent (13·8 g. per cent). E.S.R. 3 mm./hr. (Westergren). Packed-cell volume 43 per cent. W.B.C. 5000 per c.mm. normal differential. Platelets 290,000 per c.mm. Coagulation time 7½ min. Bleeding time 2 min. Hess's test—very strongly positive. E.C.G. normal. Capillary fragility test strongly positive. Blood-culture sterile. Urine qualitative chromatogram: No 5 hydroxyindole acetic acid or other abnormality detected. Indoxyl sulphate and tryptophane present in normal concentration. Myelogram—showed partial obstruction on the left lateral aspect of the cord opposite the bodies of C.3, 4, and 5. The appearances favoured an extradural mass on the left side displacing the cord and its membranes. An extradural hæmatoma was suspected.

At Operation (May 3, 1956).—The old cervical wound was reopened, the cord was surrounded posteriorly and to the left side by dense scar tissue ¾ in. in thickness, which bulged into the cord from the left side causing displacement of the cord. The dura mater was enveloped in the fibrous tissue. The cord was mobilized as much as possible, it appeared pale, and there was no localized hæmorrhage. Closure was routine except for the dura, which could not be identified.

Post-operative Course.—The immediate recovery was satisfactory, but she developed a cerebrospinal fluid leak from the wound two days after operation which persisted for a week until the wound was partially reopened and the sinus closed. The following day the patient developed a *B. coli* meningitis which responded to intrathecal streptomycin; in three days the C.S.F. was sterile and the patient appeared to be progressing well until May 21, 1956, when she died suddenly following a massive hæmatemesis.

Post-mortem Findings.—The body was externally normal, slim, well covered. The heart, lungs, liver, kidneys, and spleen were normal. The stomach and upper small intestine contained a considerable amount of blood. The gastric mucosa showed numerous pin-point areas of hæmorrhage, otherwise it was normal.

Brain and meninges: There was generalized hyperæmia of the pia and arachnoid which was considered due to the subsiding meningitis. There was no purulent exudate and the brain was normal.

Spinal cord and meninges: There was slight hyperæmia of the piarachnoid. The spinal cord showed localized softening of the 3rd, 4th, and 5th cervical segments. Histologically the cord contained a small scar about 1 mm. diameter just lateral to the right posterior horn of grey matter, otherwise it was normal.

DISCUSSION

This case presents many interesting features. Although congenital heart disease and subacute bacterial endocarditis had been suspected on several occasions they had never been confirmed during life and there was no evidence of cardiac disease at autopsy. There was no family history of bleeding disease. The tendency to excessive bleeding had been present for many years, but repeated examination of the blood failed to show any abnormality except for one occasion when the bleeding time was prolonged. The tourniquet test had, however, been consistently positive. No vascular malformation was observed at operation to account for the hæmatomyelia, nor was there any post-mortem evidence of syringomyelia. It is therefore reasonable to postulate that this patient suffered from a primary defect of the capillaries and that the recurrent bleeding—the menorrhagia, the hæmatomyelia, and the terminal hæmatemesis—was due to this cause, although it seems likely that the latter complication was precipitated by the acute meningeal reaction.

The findings in this case approximate to those described as occurring in vascular hæmophilia, which should not be confused with hereditary pseudohæmophilia or Von Willebrand's disease (Singer and Ramot, 1956). In the latter disease there is a tendency to bleed from the nose, gums, uterus, stomach, intestines, urinary tract, and into the joints. The bleeding time is prolonged and the tourniquet test is positive, but the coagulation time, clot retraction, the platelets, and the blood constituents are all normal; the spleen is not enlarged (Whitby and Britton, 1950; Wintrobe, 1951). According to Whitby and Britton (1950) the essential abnormality is delayed agglutination of the platelets. Macfarlane (1941), however, maintains that the capillaries are distorted and are lacking on contractile power in pseudohæmophilia.

Treatment.—The treatment of this condition remains at present essentially symptomatic and consists of dealing with the complications as they arise. The highly satisfactory recovery, which was complete, following laminectomy and aspiration was gratifying in this case; other similar cases have been recorded (Wyburn-Mason, 1943), but such a complete recovery is unusual.

Blood transfusions proved of value given during operation and the various major procedures were accomplished without excessive blood-loss. Their effect appears of temporary value only and is not curative. Cold blood transfusion has also been advocated (Singer and Ramot, 1956). The use of cortisone and adrenoxyl (adrenochrome, monosemicarbazone dihydrate) was considered, but they were not employed when it was found that their administration produced no effect on the result of the tourniquet test. Leaving the dura mater open is usually considered a wise precaution in these cases, but in this particular case it led to considerable difficulties at the second spinal exploration. The excessive amount of scar tissue found at the second operation makes one wonder if there is any relationship between the capillary disease and its increased formation.

SUMMARY

1. A case of vascular pseudohæmophilia is presented in which a primary defect of the capillaries is held responsible for the recurrent episodes of bleeding culminating in a hæmorrhage into the spinal cord.

2. The satisfactory recovery following laminectomy and aspiration of the hæmatomyelia is described.

3. It is uncertain whether there is any association between the vascular pseudohæmophilia and the liability to excessive fibrous tissue formation which was responsible for the partial compression of the spinal cord.

4. No treatment of the underlying vascular disease proved of permanent value although blood transfusion enabled two major operations to be successfully accomplished. The treatment of the complications is discussed.

Acknowledgements.—I am grateful to Dr. J. D. N. Nabarro for advice in the management of the medical aspects of this case; and to Dr. P. H. Buxton for the post-mortem report.

REFERENCES

BERKLEY, H. J. (1889), *Brain*, **12**, 460. (Quoted by KINNIER WILSON.)
BUCKLEY, A. C. (1936), *J. nerv. ment. Dis.*, **83**, 422.
DANA, C. L. (1894), *Ibid.*, **21**, 567. (Quoted by KINNIER WILSON.)
ELSBERG, C. A. (1916), *Diseases of the Spinal Cord and Its Meninges*. Philadelphia: W. B. Saunders Co.
GOWERS, W. R. (1903), *Lancet*, **2**, 993. (Quoted by KINNIER WILSON.)
MACFARLANE, R. G. (1941), *Quart. J. Med.*, **10**, 1.
SINGER, K., and RAMOT, BRACHA (1956), *Arch. intern. Med.*, **97**, 715.
WHITBY, L. E. H., and BRITTON, C. J. C. (1950), *Disorders of the Blood*. London: J. & A. Churchill.
VON WILLEBRAND, E. A., and JURGENS, R. (1926), *Finska, läk-sallsk Landl.*, **68**, 87.
WILSON, S. A. K. (1940), *Neurology*. London: Edward Arnold.
WINTROBE, M. M. (1951), *Clinical Hæmatology*. London: H. Kimpton.
WYBURN-MASON, R. (1943), *The Vascular Abnormalities and Tumours of the Spinal Cord and its Membranes*. London: H. Kimpton.

VOLVULUS OF A JEJUNAL ENTEROGENOUS CYST AT THE AGE OF ONE MONTH

By N. F. KIRKMAN

CONSULTANT SURGEON TO THE DUCHESS OF YORK HOSPITAL FOR BABIES, MANCHESTER

THIS case is regarded as worthy of record in view of the rarity of enterogenous cysts of the jejunum. In an extensive review of the literature of intestinal reduplications and enterogenous cysts, Dohn and Povlsen (1952) found reports of 305 cases. The lower ileum was by far the commonest intestinal segment involved and the jejunum the least. Gross (1953) recorded 68 cases, of which only 3 were enterogenous cysts of the jejunum. Wangensteen (1955) has since reported another case of a jejunal enterogenous cyst.

CASE REPORT

T. G., aged 1 month, was admitted on Dec. 23, 1955, as an urgency with the complaint of projectile vomiting and constipation. He had been delivered by forceps and vomited some liquor two days after birth. He improved after the first week, for a fortnight, when short episodes of vomiting occurred. He remained fairly well after this for a few days, until twenty-four hours prior to admission when vomiting recurred and he became constipated. The vomit was projectile, and bile-stained, and occurred two hours after food. He had been fed on breast milk complemented variably with diluted full-cream National Dried Milk or glucose-water. Micturition was normal. Birth weight 7 lb. 6 oz.

ON EXAMINATION.—Temperature 98°; Pulse 136; Respiration 30. Average infant, but somewhat sunken-eyed and hungry. Eyes, ears, fauces, chest—normal. Abdomen—distended, especially in the upper half; a ladder pattern, due to visible peristalsis, could be seen, but no mass could be felt. Rectal examination revealed a small amount of dry normal stool which was passed immediately after examination.

Straight Radiograph of Abdomen.—This showed a fluid level high in the jejunum and no other air shadow could be seen in the abdomen.

A diagnosis of high small-bowel obstruction, possibly due to malrotation of the gut, was made. Intravenous drip was set up and the child prepared for operation.

AT OPERATION.—A full transverse supra-umbilical abdominal incision was made. This gave a good exposure of the upper abdominal viscera without a great deal of retraction being made. The stomach and duodenum were normal. The proximal jejunum was dilated and grossly congested for the first 8 in., where a firm cystic swelling was found in the mesentery of the jejunum; it lay behind the fundus of the stomach in the left subphrenic region. The mesenteric border of the adjacent jejunum appeared to fuse with the cyst. Distal to the cyst the jejunum and ileum were collapsed but normal. The cyst, with the adjacent bowel, had rotated on the mesentery forming a volvulus of the proximal jejunal loop, and the cyst and 8 cm. of jejunum were resected. After reduction of the volvulus the bowel was seen to be viable. An end-to-end anastomosis was made in two layers using No. 90 thread; the inner continuous and the outer one interrupted sutures. The appendix was normal and was removed. The colon was normal.

Figs. 674, 675 show the specimen removed. *Fig.* 674 shows the cyst as it appeared at operation, and *Fig.* 675 as it appeared on section.

Pathological Report (Dr. K. V. Lodge).—The specimen consists of 8 cm. of jejunum with a cyst 6·5 cm. in diameter which has been opened and appears to arise from the muscle layer of the gut. The cyst is smooth walled and unilocular.

Histological Examination: Enterogenous cyst.

The cyst wall is composed of fibrous tissue and a muscle layer continuous with that of the jejunum. The lining is fibrous tissue and there is no evidence of mucosa. There is a slight infiltration of the wall by inflammatory cells. The appearances are compatible with an enterogenous cyst.

PROGRESS.—The patient was given a post-operative blood transfusion of 80 c.c. whole blood followed by intravenous saline and glucose-water for 48 hours, by which time normal bowel action had returned and oral feeding was started. He was discharged home on the seventh post-operative day as his mother was a trained nurse and was able to breast-feed him. He was seen

subsequently in the Out-patient Department after two months and was quite well, feeding normally, and gaining weight.

DISCUSSION

These cysts are of interest from the standpoint of their aetiology, diagnosis, and treatment. Bremer (1944) has put forward what appears to be the most satisfactory theory to account for their origin, and his views are supported by several recent reviews of the subject (Gross, 1953; Moore and Battersby, 1952; and Boyd, 1955). Bremer differentiates between the origin of enterogenous cysts and that of more complete reduplications of the gut. He states that enterogenous cysts arise from transient, primitive diverticuli which appear on the antimesenteric border of the gut in the eighth week (20-mm. embryo). Lewis and Thyng (1907) and Evans and Keith (1929) have also noted the occurrence of these transient diverticuli. Normally the diverticuli disappear in a week or so, but very rarely they persist and the tip of a diverticulum may be sequestrated to form a sequestration cyst by the growing muscle layer of the bowel wall. This is believed to account for the origin of the majority of enterogenous cysts, but Bremer considers that they may also arise very rarely from irregularities in the vacuolation of the intestinal mucosa which occurs normally in the sixth week or 10-mm. stage. This irregular vacuolation, however, is more usually responsible for longer reduplication of gut. Enterogenous cysts may occur at any site from the tongue to the anus.

Enterogenous cysts are rarely diagnosed preoperatively, unless they are palpable. More usually these cases present with signs of intestinal obstruction before the age of 1 year. Often recurrent attacks of colic associated with melæna and anæmia occur (Moore and Battersby, 1952; Edwards, 1929).

Dohn and Povlsen (1952) point out in their review that the diagnosis of enterogenous cyst is probable in an infant having signs of intestinal obstruction associated with a mobile, rounded, cystic abdominal swelling when an ovarian swelling can be excluded. Of the cases they traced 60 per cent had intestinal obstruction and 25 per cent of all cases were fatal.

Most of the cases of enterogenous cyst are operated on for intestinal obstruction in infancy. When the cyst is found it should, if possible, be resected with the adjacent intestine, because the mucosal wall of the cyst is frequently continuous with that of the bowel and often the two structures have a common blood-supply, as occurred in the case reported here. It may be difficult or impossible to dissect the cyst away from the gut—a factor, therefore, in increasing the length of the operation, and correspondingly the mortality of the operation, if the attempt is made.

With this proviso, there seems no reason why the treatment of enterogenous cysts will not yield better results than previously reported now that fluid and electrolyte therapy are better understood in pædiatric practice.

FIG. 674.—The cyst and the attached jejunum as removed at operation.

FIG. 675.—The enterogenous cyst on section. Note the reduced lumen of the jejunum where the cyst arises from the jejunal wall.

REFERENCES

BOYD, W. (1955), *Pathology for the Surgeon*, 7th ed., 202. Philadelphia: W. B. Saunders Co.

BREMER, J. L. (1944), *Arch. Path. (Lab. Med.)*, **38**, 132.

DOHN, K., and POVLSEN, O. (1952), *Acta chir. Scand.*, **102**, 21.

EDWARDS, H. (1929), *Brit. J. Surg.*, **17**, 7.

EVANS, A., and KEITH, A. (1929), *Brit. J. Surg.*, **17**, 35.

GROSS, R. E. (1953), *Surgery of Infancy and Childhood*, 221. Philadelphia: W. B. Saunders Co.

LEWIS, F. T., and THYNG, F. W. (1907), *Amer. J. Anat.*, **7**, 505.

MOORE, T. C., and BATTERSBY, J. S. (1952), *Surg. Gynec. Obstet.*, **95**, 557.

WANGENSTEEN, O. H. (1955), *Intestinal Obstructions*, 3rd ed., 449. Springfield, Ill.: Charles C. Thomas.

REVIEWS AND NOTICES OF BOOKS

Anatomie et Chirurgie du Péricarde. By HENRI MILHIET and PAUL JAGER, with a Foreword by J. BAUMANN. 11 × 8¾ in. Pp. 292, with 145 illustrations. 1956. Paris: Masson. 4,000 fr.

THIS monograph deals, in its first part, with the embryology and anatomy of the pericardium in great detail; 175 pages are devoted to this. All thoracic and cardiac surgeons will find this section invaluable, both for reading and for reference.

The second part, another 110 pages, deals with the surgical anatomy of the pericardium, especially the intrapericardial exposure of the vessels.

Both parts are freely and beautifully illustrated. The monographs can be confidently recommended to all those who are engaged in thoracic and cardiac surgery.

Companion in Surgical Studies. By IAN AIRD, Ch.M., F.R.C.S., Professor of Surgery in the University of London. Director of the Surgical Unit, Postgraduate Medical School of London, Hammersmith Hospital, W.12. Second edition. 9¾ × 7¼ in. Pp. 1302 + xii. 1957. Edinburgh: E. & S. Livingstone Ltd. 84s.

WHEN we reviewed the first edition of this work in 1949 we had nothing but praise for it, and to-day Professor Aird has again produced a book of outstanding merit. It is impossible to review this volume in detail because of its large size, but it certainly does cover the wide field of general surgery in a masterly fashion and every rare surgical condition is also adequately dealt with. A very comprehensive list of references is incorporated, and as these references for the most part deal with recently published papers, they enhance the value of the work and make it a reference volume.

We wish to reiterate the opinion we expressed previously regarding the first edition—namely, " that this book is a credit to the surgical literature of England ".

Lymphatics, Lymph and Lymphoid Tissue. By JOSEPH MENDIL YOFFEY, D.Sc., M.D. (Manch.), F.R.C.S. (Eng.), Professor of Anatomy, University of Bristol; and FREDERICK COLIN COURTICE, M.A., D.Phil. (Oxon.), D.Sc. (Sydney), F.R.A.C.S. (Hon.). 9½ × 6 in. Pp. 510 + viii, with 99 illustrations. 1956. London: Edward Arnold (Publishers) Ltd. 60s.

THIS volume gives an account of the lymphatic system, following the path originally illuminated by the late Dr. Drinker. The modifications of lymphoid tissue are traced through the vertebrates and it is pointed out how in mammals the separation of lymphoid from myeloid tissue reaches its acme in the development of the lymph-node. Only in the higher vertebrates are there lymph-nodes as well as lymph-vessels, and it would seem from the point of view of comparative anatomy that it is almost a matter of chance that these two parts of the lymphatic system have become associated.

The thesis of the work is that the function of lymph is to return large protein molecules to the blood-stream. In discussing lymphatic tissue three distinct types are considered: the lymph-nodes with their afferents and efferents; the lymphoid tissue in mucous membranes which possess efferents only; and the spleen, where the lymphoid tissue is within the blood-stream and there are neither afferents nor efferents. The part played by the bone-marrow is fully discussed. The structure of the lymph-gland is described and the function of the germinal centres is held to embrace more than the manufacture of lymphocytes.

Much attention is paid to the permeability of the capillary walls, especially to lipid insoluble molecules which depend for their passage through these walls on their size, no loss of energy being involved in the process. 'The Pore Theory' and the views of Starling on these problems are fully discussed.

The various regions of the body are considered in relation to the function of the lymph within them and the part played by the lymph in the absorption of digested products from the small intestine is described.

There is a short section dealing with the effect on lymphoid tissue of ionizing radiations. The functions of lymphoid tissue as a defensive mechanism involves a description of the 'barrier theory', whereby, for instance, the tonsils are held to be the guardians of the intestinal tract, and it is pointed out how simple filtration of bacteria and inflammatory debris cannot account for the whole part which this tissue plays in defence. It is argued that the lymphoid tissue is a source of antibody and that these antibodies may well be elaborated by the plasma cells. For want of definite evidence, one way or the other, no consideration is given to the possible endocrine function of the lymphatic glands. The circulation of the lymph is fully considered and it is maintained that the vast majority of the lymphocytes entering the blood-stream from the thoracic duct are new-formed, and that lymphatic circulation through the blood-stream and back to the lymphatics is practically non-existent.

Radio-active isotope studies were conducted to estimate the life span of a lymphocyte, which most observers regard as being of the duration of a few days, but estimates are very variable and range from two to two hundred days. The interesting theory of Andrew and Andrew is discussed—namely, that some of the dermal lymphocytes may be converted into epithelial cells and play a part in the regeneration of epithelial structures. The fate of lymphocytes is in fact somewhat obscure. No doubt some disintegrate in the blood-stream and others are excreted into the intestine. This, however, would appear to be a branch of study which offers considerable interest in the future.

There is a discussion on the possibility of transformation of lymphocytes into plasma cells, macrocytes, microphages, fibroblasts, myeloblasts, etc., and in the final chapter there is an account of the practical considerations relating to œdema, ascites and the spread of infection.

This work is essential for those interested in the study of the lymphatic system. It is beautifully produced, clearly illustrated, and reasonably priced.

Medical Negligence. By The Right Hon. LORD NATHAN, P.C., Chairman of the Board of Governors of Westminster Hospital, with the collaboration of ANTHONY R. BARROWCLOUGH, B.A., of the Inner Temple, Barrister-at-Law. 8¾ × 5½ in. Pp. 218 + xxxii. 1957. London: Butterworth & Co. (Publishers) Ltd. 35s.

THIS is a book which should prove of real value to surgeons in this age of litigation. It is in fact an account of the law of negligence in relation to the medical profession and hospitals.

Many cases of negligence are cited and explained. The liabilities of the surgeon and staff during operations

are set out and explained in detail. The duty of the surgeon in regard to 'swab cases' is set out and discussed. The question of damages, and how they are related to the various cases of negligence, is set out in a lucid manner.

Lord Nathan has produced an excellent volume for which the medical profession as a whole will indeed be grateful.

Modern Operative Surgery. Edited by the late G. GREY TURNER and LAMBERT CHARLES ROGERS, Professor of Surgery, University of Wales. With a Foreword by Sir GORDON GORDON-TAYLOR, K.B.E. Fourth edition. In two volumes. 9 × 6½ in. Vol. II. Pp. 1383 + xii, with 614 illustrations. 1956. London: Cassell & Co. Ltd. 75s.

THE second volume of the fourth edition of this well-known surgical work deals with many sections of surgery. Naunton Morgan and Lloyd Davies's section on operation on the rectum and anal canal is excellent and should prove of real worth to all surgeons who have to perform operations on the rectum. Professor Windeyer's contribution on radiotherapy in malignant disease is masterly.

Geoffrey Jefferson, writing on operations on skull and brain, has given an up-to-date account of the surgery of the brain.

Another outstanding section is the chapter devoted to the surgery of the thyroid, parathyroid, and thymus glands contributed by Geoffrey Keynes.

There can be little doubt that this work will continue to take its place as a useful treatise on operative surgery as practised in England, but there is still too much obsolete material which should be eliminated and too many old and dated illustrations.

We hope Professor Lambert Rogers will exert his influence with the publishers when the next edition is required.

Operating Room Technic, St. Mary's Hospital, Minnesota. Fifth edition. 8⅛ × 5⅛ in. Pp. 359 + xiv, with 218 illustrations. 1957. Philadelphia and London: W. B. Saunders Co. 52s. 6d.

THE new fifth edition of this useful and practical guide to theatre nurses has been very extensively revised and largely rewritten so as to incorporate all the new operations on the heart, lungs, brain, and spinal cord.

Although written for nurses, it should prove of value to the medical student who wishes to become familiar with the general procedure of operations. The various instruments used, the position of the patient, and a précis of the stages of the operation are given and illustrated.

Illustrations of all the various instruments used in operations are appended at the end of the book.

The Management of Abdominal Operations. Edited by RODNEY MAINGOT, F.R.C.S., Surgeon to the Royal Free Hospital. Second edition. In two Volumes. 9⅜ × 6½ in. Pp. 1432 + xvi, with 444 illustrations. 1957. London: H. K. Lewis. £8,

THE new second edition of this excellent work on abdominal surgery appears in two volumes, which in itself is a great advantage to the reader. Vast alterations and additions have been made and in some ways the volumes are almost new; some 200 original half-tone pictures have been incorporated in this new edition.

The usefulness of this work has been enhanced by some excellent practical chapters on such subjects as Fluid and electrolyte balance; post-operative chest complications; the role of vitamins in abdominal surgery; alkalæmia and acidæmia with special reference to abdominal cases. All these biochemical factors are becoming more and more important in the pre- and post-operative treatment of abdominal cases.

Volume I is devoted to general considerations in abdominal operations, and every aspect has been amply covered. Volume II contains articles dealing with regional considerations, including a splendid chapter on the management of abdominal injuries in warfare and in civil life. This chapter comes from the facile pen of Sir Gordon Gordon-Taylor and is a masterpiece of practical experience and lucid expresion.

We should like to congratulate Rodney Maingot on an excellent work which will advance British surgical prestige the world over.

Essentials of Modern Surgery. Edited by R. M. HANDFIELD-JONES, M.C., M.S., F.R.C.S., Senior Surgeon to St. Mary's Hospital, Lecturer in Surgery, St. Mary's Hospital; Examiner in Surgery to the Universities of London, Leeds and Manchester, and Sir ARTHUR E. PORRITT, K.C.M.G., C.B.E., M.A., M.Ch., F.R.C.S., Sergeant-Surgeon to Her Majesty the Queen; Surgeon, St. Mary's Hospital and Royal Masonic Hospital; Examiner in Surgery, Universities of Cambridge and London. Fifth edition. 9¾ × 6 in. Pp. 1276 + xvi, with 649 illustrations, several in colour. 1957. Edinburgh: E. & S. Livingstone Ltd. 75s.

IT is some six years since the last edition of this book appeared and much has happened in the field of surgery during the interval. The editors have certainly persuaded the various contributors to thoroughly revise and bring up to date their various sections, and many new illustrations have been incorporated. Mr. J. Crawford Adams, a new contributor to the book, has largely rewritten the chapters on Fractures; and Dr. Hulbert, another new contributor, has written an entirely new section on Radiotherapy, which includes the use of radio-active isotopes.

This book, which is written essentially for medical students, has completely caught up with the changing face of surgery and we would like to congratulate the editors on their efforts to make this work worthy of British surgery. We have only one criticism and that is the large size and weight of the book; two volumes would make for easier and more comfortable reading.

Positioning in Radiography. By K. C. CLARK, M.B.E., F.S.R., Honorary Fellow and Past President, Society of Radiographers. Principal of the Department of Radiography and Medical Photography of Ilford Ltd. 11¾ × 9 in. Pp. 655, with 2150 illustrations. 1956. London: Ilford Limited. Wm. Heinemann (Medical Books) Ltd. 105s.

THE first edition of this important work appeared in 1939 and immediately became the reference volume of every X-ray department both at home and abroad. Since that date each succeeding edition has outshone the previous one, and now the seventh edition has been published. We have nothing but praise for this outstanding volume, which should prove valuable to both radiologists and radiographers alike. The new sections in this edition include chapters on myelography, miniature radiography, cineradiography, and angiography.

The clinical photographs and the radiographs could not be bettered.

An excellent production, of which the publishers may well be proud.

The Head and Neck in Roentgen Diagnosis. By EUGENE P. PENDERGRASS, M.D., Professor of Radiology, University of Pennsylvania; J. PARSONS SCHAEFFER, M.D., Ph.D., Professor of Anatomy and Director of the Daniel Baugh Institute of Anatomy, Emeritus, Jefferson Medical College; and PHILIP I. HODES, M.D., Professor of Radiology University of Pennsylvania. Second edition. In two volumes. 10¼ × 7 in. Vol. I, Pp. 878 + lv, with 960 illustrations, and 66-pp. Index to Vols. I and II; Vol. II, Pp. 879–1759 + xlii, with 780 illustrations, and 66-pp. Index to Vols. I and II. 1956. Oxford: Blackwell Scientific Publications. £14.

THE second edition of this well-known work appears in two volumes and in a changed format. This is all to the good, for it does help the reader to find the subject-matter more easily.

A large part of this work has been rewritten and much new matter has been incorporated. Many new anatomical drawings have been included and the wealth of radiographs is certainly a feature.

This work should interest the neurosurgeon, the orthopædic surgeon, as well as the general surgeon and the plastic surgeon, for it contains a wealth of information and is certainly a great contribution to medical literature.

The Treatment of Fractures. By LORENZ BÖHLER, M.D., Director of the Accident Hospital, Vienna; Professor of Accident Surgery, University of Vienna. Volume II. Translated from the 13th German Edition by OTTO RUSSE, M.D., Director of the Accident Hospital, Vienna, and R. G. B. BJORNSON, M.D., Diplomate, American Board of Radiology. 9½ × 6¾ in. Pp. 435 + viii, with numerous illustrations. 1957. New York and London: Grune & Shatton Inc. $17.50.

THE second volume of this well-known work is devoted to injuries of the hip and other joints of the lower extremity, together with fractures of the bones of the leg. The clinical pictures and radiographs throughout the book are excellent and give the reader a good idea of the results of treatment. Although at one time Böhler seemed to be very conservative in his treatment of fractures, the present volume clearly demonstrates his willingness to use operative measures in the treatment of difficult and comminuted fractures. Lane's plates, wires, and intramedullary nails are freely used. The chapter on gunshot fractures of bones is pre-eminent and the results obtained by operative treatment excellent.

Every surgeon who has the treatment of fractures under his charge would do well to have this book as a reference volume.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Outline of Fractures, including Joint Injuries. By JOHN CRAWFORD ADAMS, M.D., F.R.C.S., Consultant Orthopædic Surgeon, St. Mary's Hospital, London, and St. Vincent's Orthopædic Hospital, Pinner. 8¾ × 5½ in. Pp. 248 + viii, with 218 illustrations. 1957. Edinburgh: E. & S. Livingstone Ltd. 27s. 6d.

Chirurgie Orthopedique des Paralysies. By R. MERLE D'AUBIGNÉ, Professeur de Clinique chirurgicale orthopédique et réparatrice à la Faculté de Médecine de Paris; J. BENASSY, Chirurgien-Assistant des Hôpitaux de Paris; and J. O. RAMADIER, Chirurgien-Assistant des Hôpitaux de Paris, and 12 collaborators. 10 × 6½ in. Pp. 432, with 171 illustrations. 1956. Paris: Masson. Paper covered: 4,200 fr. Board covered: 5,000 fr.

Alfred Hospital Clinical Reports. Edited by R. S. LAWSON. Sixth edition. 10 × 6 in. Pp. 143, with numerous illustrations. 1956. Melbourne: The Alfred Hospital.

Rectoscopie Sigmoïdoscopie. By P. HILLEMAND, R. CATTAN, A. LAMBLING and A. BENSAUDE. Third edition. 11 × 7½ in. Pp. 270, with 127 illustrations, 39 in colour. 1957. Paris: Masson. Paper covered: 6,500 fr. Board covered: 7,400 fr.

Intestin Grêle Côlon-Rectum. By GUY ALBOT, et al. 10 × 6½ in. Pp. 362, with 168 illustrations. 1957. Paris: Masson. 3,400 fr.

Cleft Lip and Palate. By W. G. HOLDSWORTH, F.R.C.S., Surgeon, Rooksdown House, Basingstoke; Consultant in Plastic Surgery, South-West Metropolitan Hospital Region. With a Foreword by Sir HAROLD GILLIES, C.B.E., F.R.C.S. Second edition. 10 × 7¼ in. Pp. 187 + xii, with 146 illustrations. 1957. London: Heinemann (Medical Books) Ltd. 42s.

The Cytology of Effusions in the Pleural, Pericardial and Peritoneal Cavities. By A. I. SPRIGGS, D.M.(Oxon), M.R.C.P., with coloured drawings by GERETH M. SPRIGGS. 10 × 7¼ in. Pp. 71, with 40 illustrations, several in colour. 1957. London: Heinemann (Medical Books) Ltd. 42s.

Lumbar Puncture and Spinal Analgesia. By Sir ROBERT MACINTOSH, M.A., D.M., F.R.C.S.(Edin.), F.F.A.R.C.S., Nuffield Professor of Anæsthetics at University of Oxford. Second edition. 8¾ × 6 in. Pp. 142 + viii, with 110 illustrations. 1957. Edinburgh: E. & S. Livingstone Ltd. 25s.

Injuries of the Hand. By RONALD FURLONG, F.R.C.S., Assistant Orthopædic Surgeon, St. Thomas's Hospital; Orthopædic Surgeon, Rowley Bristow Hospital, Pyrford and Queen Victoria Hospital, East Grinstead. 10 × 6½ in. Pp. 215, with 99 illustrations. 1957. London: J. & A. Churchill Ltd. 36s.